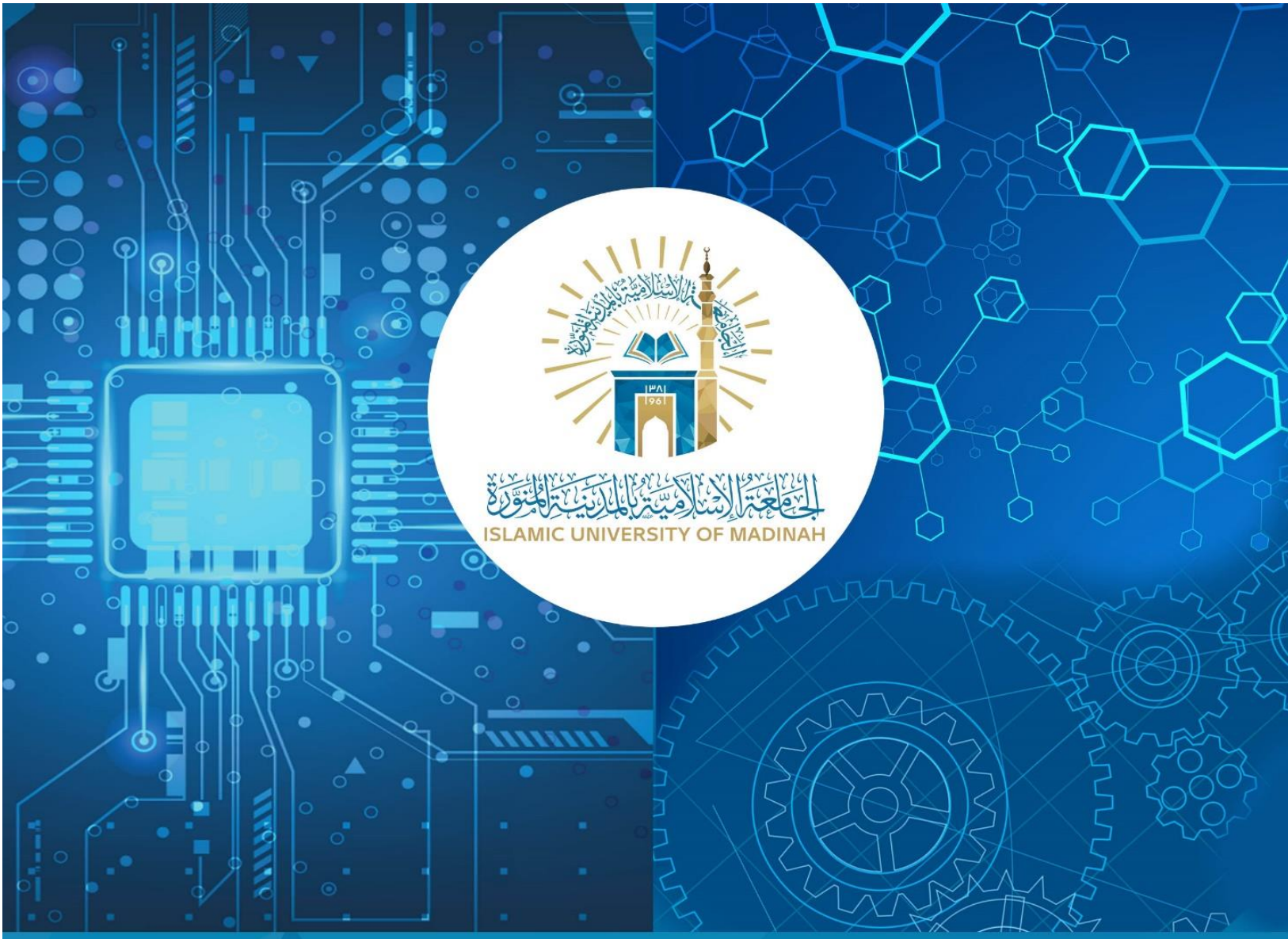


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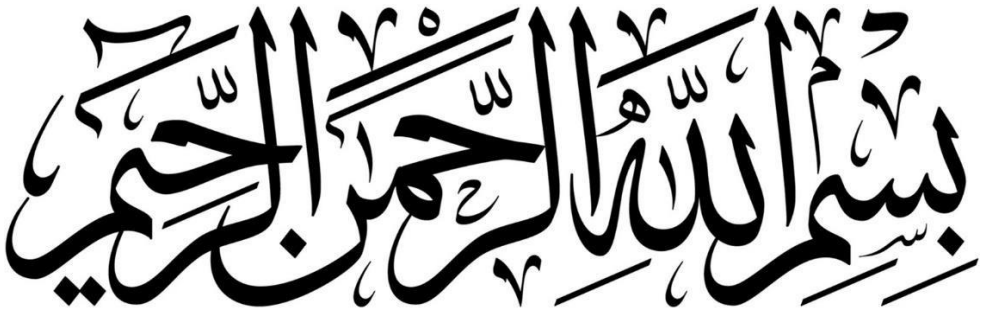
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# Tetra(4-aminophenyl) porphyrin-based Covalent Organic Frameworks

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**Abstract:** Covalent Organic Frameworks (COFs) are robust crystalline porous materials with unique properties and have promising applications in many fields such as gas adsorption, sensing and catalysis. COFs properties can be tailored by the judicious choice of their building units. Stemming from its unique properties, rigid structure and synthetic accessibility, tetra(4-aminophenyl)porphyrin (TAPP) has been employed as a building unit to construct various COF materials. This review highlights the different synthetic approaches that were exploited by researchers to assemble COF materials based on TAPP.

**Keywords**: Porphyrins; Covalent Organic Frameworks; Porous Organic Polymers; Imide; Imine.

## الهياكل العضوية التساهمية القائمة على البورفيرين Tetra(4-aminophenyl)

**الملخص:** الأطر العضوية التساهمية (COFs) هي مواد بلورية قوية مسامية ذات خصائص فريدة ولها تطبيقات واعدة في العديد من المجالات مثل امتصاص الغاز والاستشعار والحفز. يمكن تصميم خصائص COFs من خلال الاختيار الحكيم لوحدات البناء الخاصة بهم. تم استخدام البورفيرين رباعي (4-أمينوفينيل) بورفيرين (TAPP) كوحدة بناء لبناء مواد COF المختلفة ، نظرًا لخصائصه الفريدة وهيكله الصلب وإمكانية الوصول إليه الاصطناعية. تسلط هذه المراجعة الضوء على الأساليب التركيبية المختلفة التي استغلها الباحثون لتجميع مواد COF بناءً علىTAPP .

## 1. Introduction.

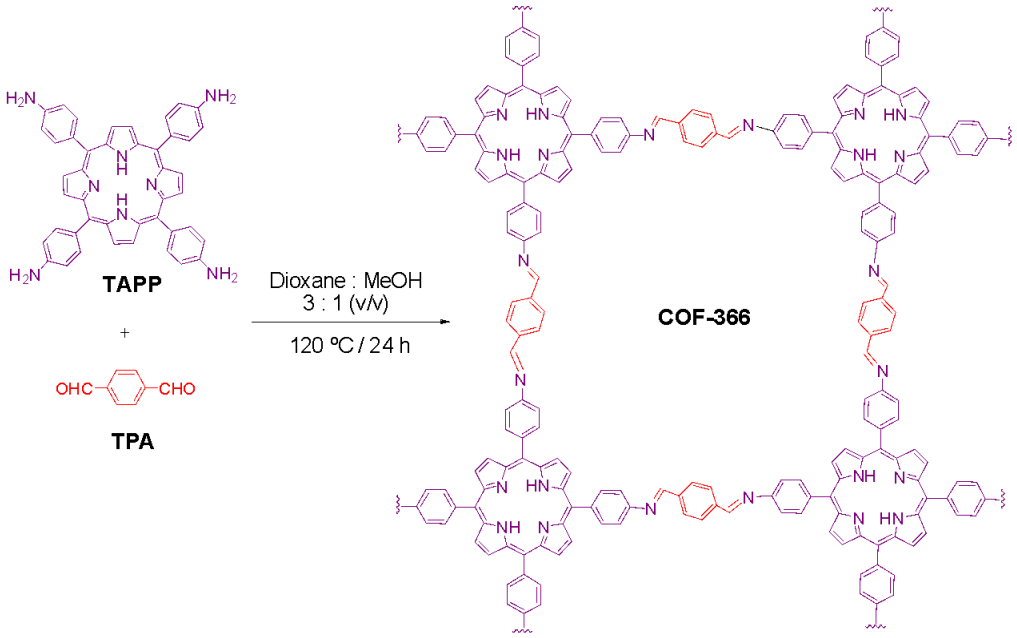
Covalent Organic Frameworks (COFs) are emerging class of crystalline porous organic materials that have attracted the interest of researchers worldwide owing to their potential applications in a large variety of domains, such as gas adsorption and separation, chemosensors, heterogeneous catalysis, energy storage and optoelectronics [1-3]. Based on reticular chemistry, COFs are constructed by the integration of organic building blocks by strong covalent bonds to make highly porous materials with predictable structures. The pore dimensions as well as the skeletons of COFs can be tailored by the judicious predesign of the knots and linkers whose symmetries determine the COFs shape and whose dimensions dictate COFs pore sizes. Owing to their excellent thermal and chemical stabilities as well as synthetic accessibility, COFs are considered an attractive alternative to MOFs (Metal Organic Frameworks) [4]. Various organic molecules have been applied as building units to construct wide range of COFs. Among these molecules, porphyrin macrocycles are considered attractive building units for making COFs owing to their rigid structures, synthetic accessibility, as well as broad-ranging optoelectronic and catalytic properties that could be tuned by substituent effects and incorporation of various metals in porphyrin macrocycle. Consequently, various porphyrin derivatives have been applied as building block to make a wide-range of porphyrin-based COFs [5] among which tetra(4-aminophenyl)porphyrin (TAPP) has been one of the most used building unit to construct COFs since the pioneering work by Yaghi's group [6]. This review summarizes the common approaches the were employed by researchers to construct COFs by using tetra(4-aminophenyl)porphyrin (TAPP) as a building unit. As shown in scheme 1, the four

amino groups of TAPP have been harnessed to construct various COFs through two main synthetic strategies, namely, formation of imine- or imide-bonds.

## 2. Synthesis of TAPP-based COFs.

### 2.1. Imine-linked porphyrin COFs.

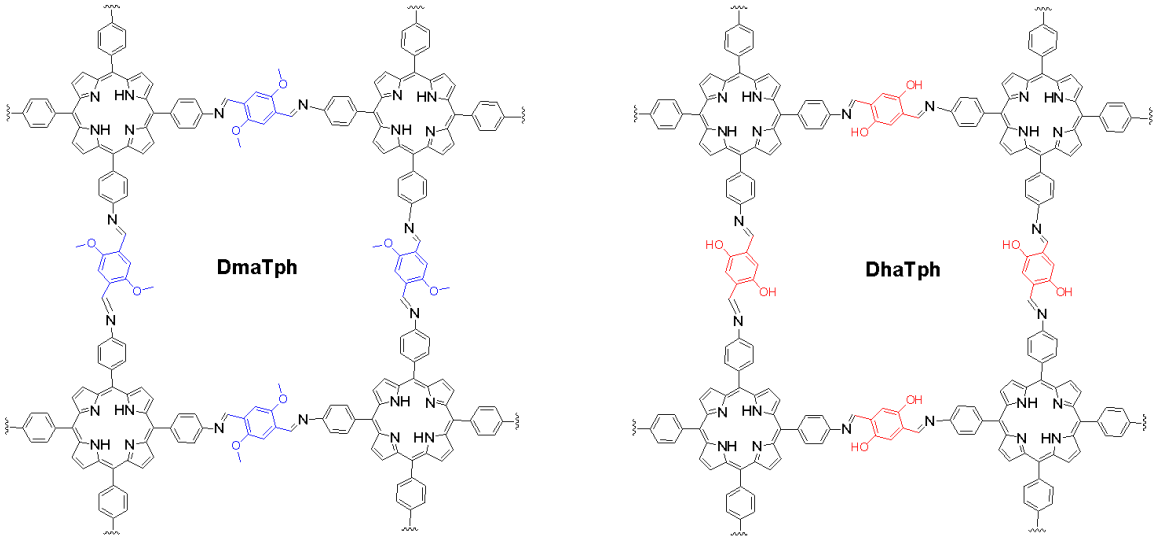
The reversible condensation between amines and aldehydes is one of the oldest reactions in organic chemistry. The dynamic nature of this reaction allows "error checking" and "proof-reading" of the resulting materials. Yaghi's group harnessed the condensation between TAPP and terephthaldehyde to construct imine-linked porphyrin COFs known as COF-366 by solvothermal reactions. As shown in scheme 1, COF-366 has square channels with porphyrin moieties located at the nodes of the square skeletons and are linked by the imine-bonds [7].




**Scheme 1**. The synthesis of COF-366.

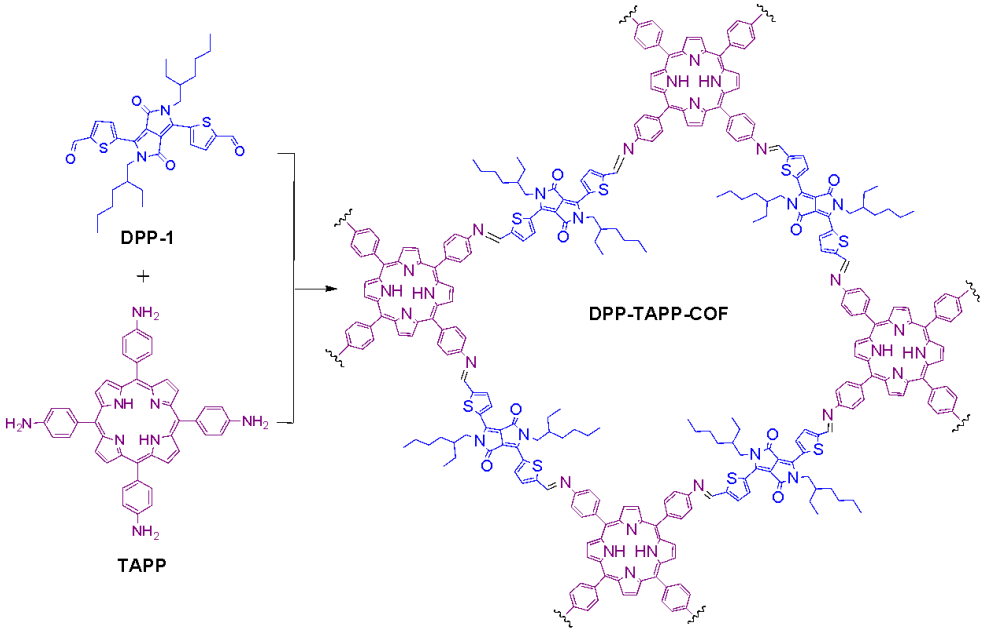
Later on, the effect of incorporating hydrogen bonding on the stability of the resulting imine-linked COFs was investigated through the synthesis of DmaTph and DhaTph via the condensation of TAPP with either 2,5-dimethoxyterephthaldehyde or 2,5-dihydroxyterephthaldehyde, respectively [8].

It was concluded that, DhaTph exhibits higher thermal, water, and acid stability than DmaTph owing to the OH….N=C intramolecular hydrogen bonding within the DhaTph structure (scheme 2).



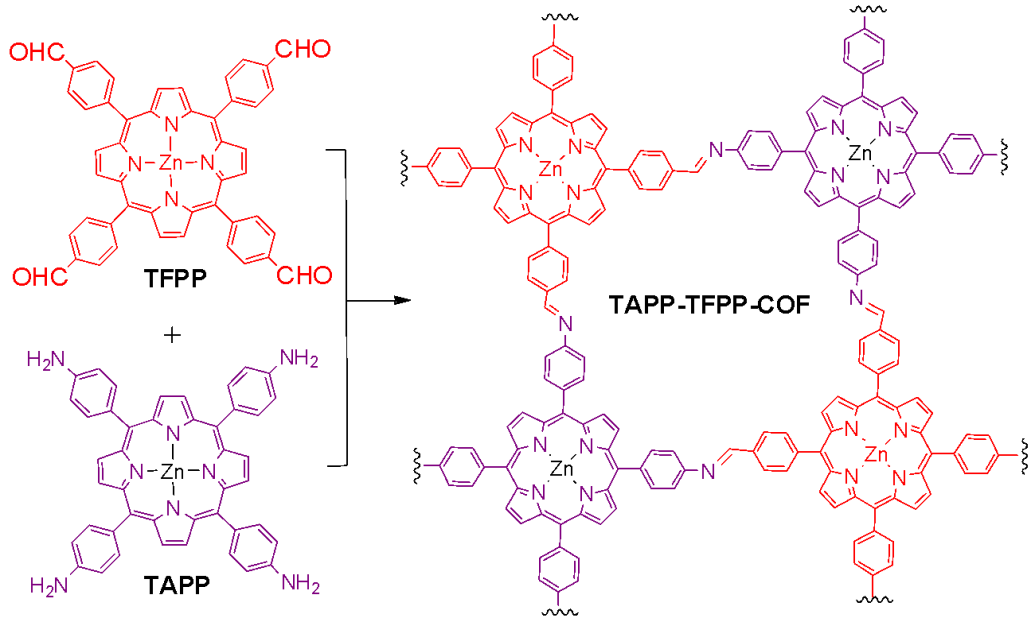

**Scheme 2**. Structures of imine-linked DmaTph and DhaTph porphyrin COFs.

In another report, Beuerle et al. exploited the condensation between TAPP and a diketopyrrolopyrrole (DPP) to assemble a novel imine-linked porphyrin COFs (DPP-TAPP-COF) with an enhanced absorption capability up to 800 nm [9]. Furthermore, the resulting COF self-assembles into a hollow microtubular with outer and inner tube diameters of around 300 and 90 nm, respectively (scheme 3).



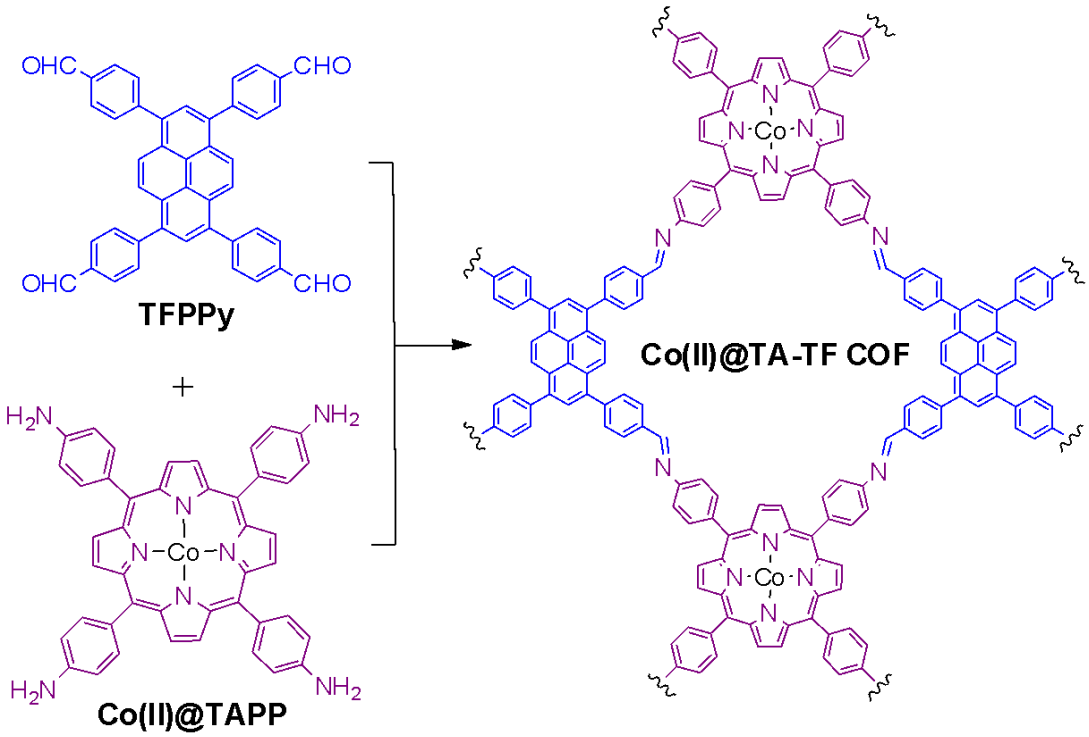
**Scheme 3**. Synthesis of DPP-TAPP-COF.

Huang et al. reported the synthesis of another imine-linked porphyrin COF (TAPP-TFPP-COF) through the condensation between TAPP and tetra(4-formylphenyl)porphyrin TFPP under typical solvothermal conditions (scheme 4) [10]. The resulting COF has a tetragonal micropores at a size of 1.8 nm and exhibited high crystallinity, excellent stability, and good porosity. In addition, the conductivity of TAPP-TFPP-COF can be greatly enhanced after doping with iodine.




**Scheme 4.** Synthesis of TAPP-TFPP-COF.

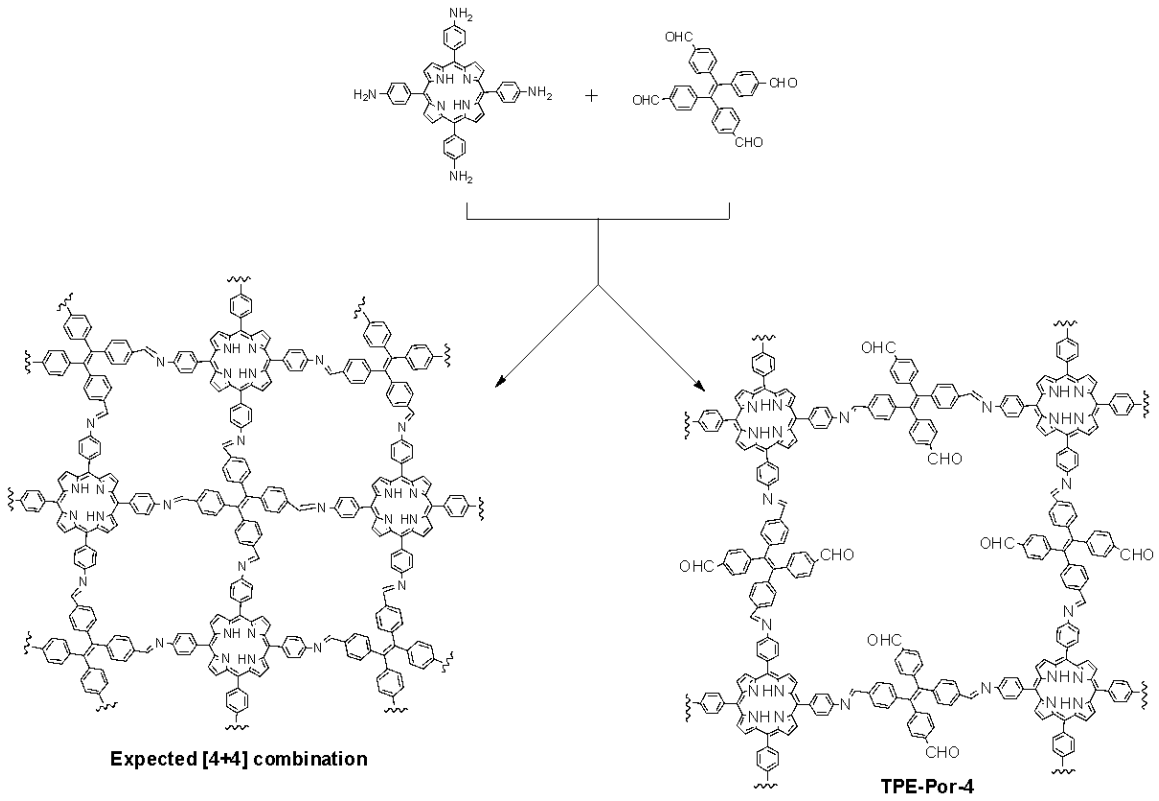
Recently, Gao et al. reported the synthesis of another imine-linked porphyrin COF, termed Co(II)@TA-TF COF by the solvothermal reaction of cobalt(II) TAPP and 1,3,6,8-tetrakis(4-formylphenyl)pyrene (TFPPy) (scheme 5) [11]. The resulting Co(II)@TA-TF COF possesses micropores suitable for $CO_2$ adsorption owing to the alternate stacking of the building units, and was equipped with cobalt(II) porphyrin units as catalytic sites into the vertices of the layered tetragonal networks that enable the conversion of $CO_2$ into cyclic carbonates under mild conditions.




**Scheme 5**. Synthesis of Co(II)@TA-TF COF.

Chen et al. reported a recent imine-linked porphyrin COF, termed TPE-Por-4, by the condensation of TAPP and 4,4',4'',4'''-(ethene-1,1,2,2-tetrayl)tetrabenzaldehyde ($D_{2h}$-symmetric) [12]. The expected route for the [4+4] condensation was not observed based on a series of structure characterization of TPE-Por-4 (scheme 6). The resulting COF suspension shows unique fluorescent properties originated from its building units and displays an apparent response to pH fluctuation ranging from 2 to 4, rendering it suitable for spectroscopic monitoring of medium pH value.

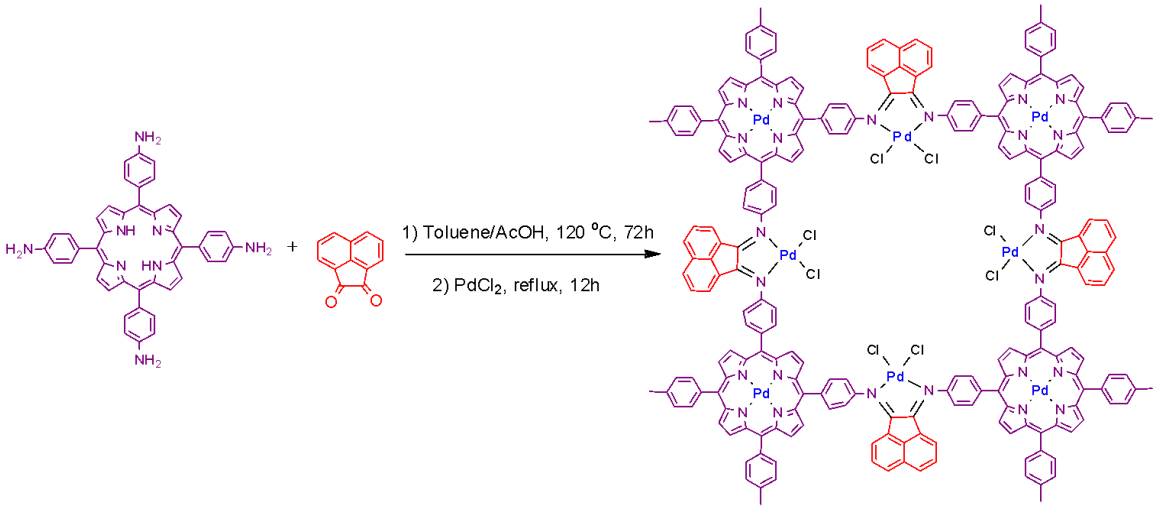
In another approach, Gu et al. constructed a novel imine-linked porphyrin COF, termed PPOP-1(Pd), first, via imine condensation of TAPP and acenaphthalenequinone followed by refluxing with $PdCl_2$ to afford PPOP-1(Pd) (scheme 7) [13]. The resulting COF contains two catalytic sites, namely, Pd(II)-porphyrin and Pd(II)-α-diimine moieties rendering it efficient for tandem catalytic reactions.



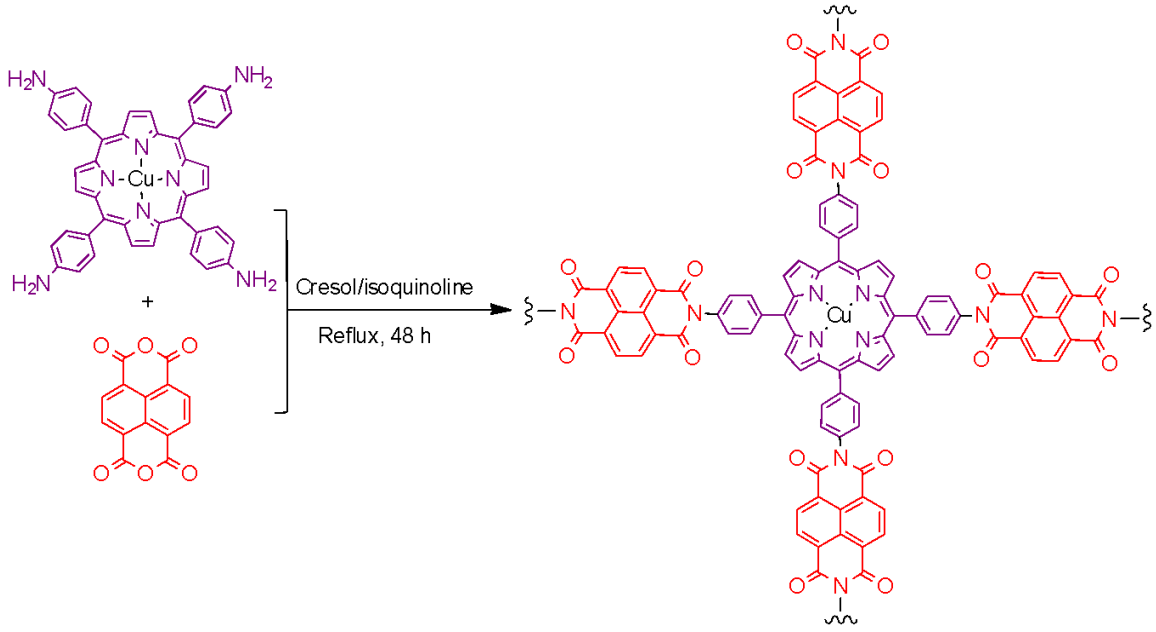

**Scheme 6**. Synthesis of TPE-Por-4.

## 2.2. Imide-linked porphyrin COFs.

Polyimide (PI) polymers are known for their excellent chemical and thermal stabilities. Typically, imidization reaction involves the condensation of an amine and an anhydride. The imidization reaction has been exploited to construct various porphyrin COFs in which TAPP (amine monomer) was employed as a node and the anhydride monomer as a linker. For instance, Echegoyen et al. reported the synthesis of a polyimide porphyrin COF via the condensation of Cu (II)-TAPP and naphthalene tetracarboxylic dianhydride in m-cresol/isoquinoline mixture (scheme 8) [14]. The resulting polyimide porphyrin COF exhibited adsorption capacity of 3.5 wt% for $CO_2$, 0.32 wt% for $CH_4$ at 273K, 1bar, and 0.4 wt% for $H_2$ at 77 K/1 bar.



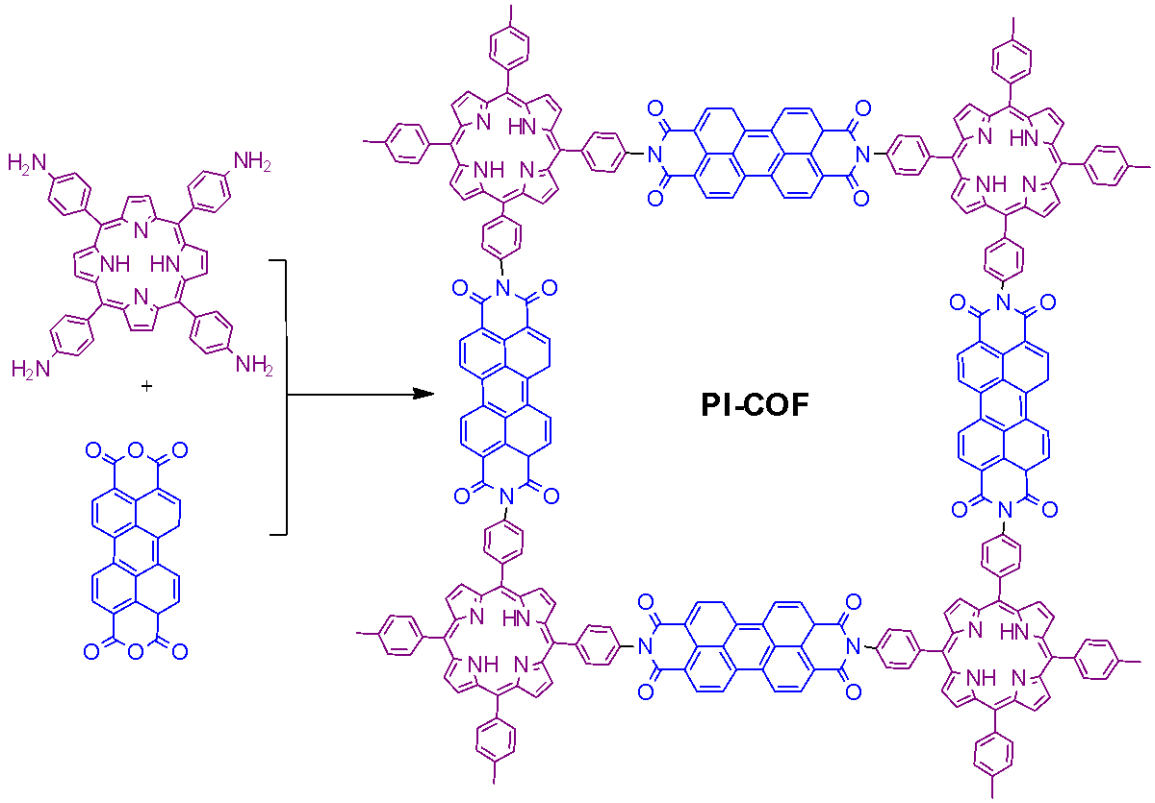

**Scheme 7**. Synthesis of PPOP-1(Pd).




**Scheme 8**. Synthesis of Cu(II)-TAPP and naphthalene tetracarboxylic dianhydride based COF**.**

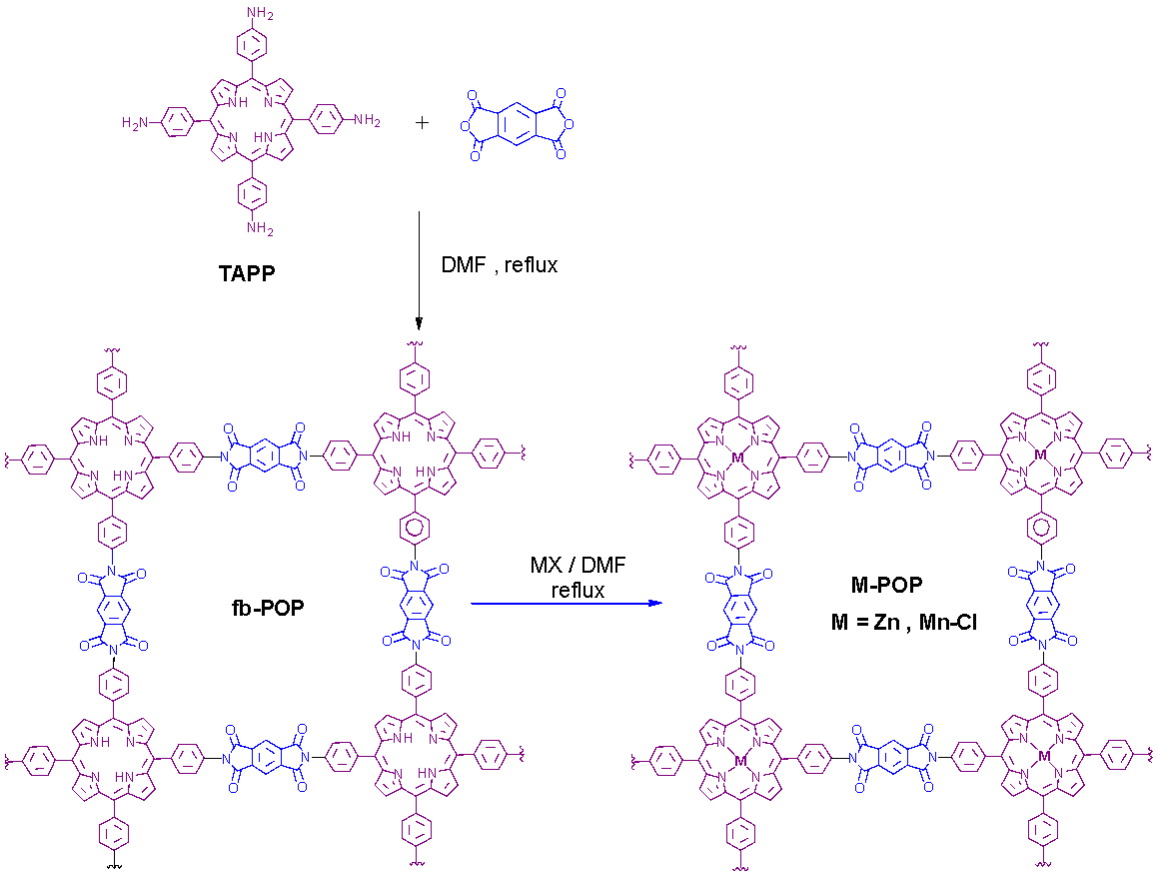
Another polyimide porphyrin COF, termed PI-COF, was constructed by Xian et al. via the imidization reaction of TAPP and perylenetetracarboxylic dianhydride (PTCA) (scheme 9) [15]. The resulting PI-COF possesses porous crystalline and excellent thermal stability. Furthermore, it exhibits a strong fluorescence which was attributed to the existence of a p-n heterojunction between TAPP and PTCA building units. The fluorescence was enhanced upon the exfoliation of PI-COF to

few layered PI covalent organic nanosheets (PI-CONs). The latter was employed as a fluorescent probe to detect TNP with high sensitivity and selectivity.




**Scheme 9**. The synthesis of PI-COF.

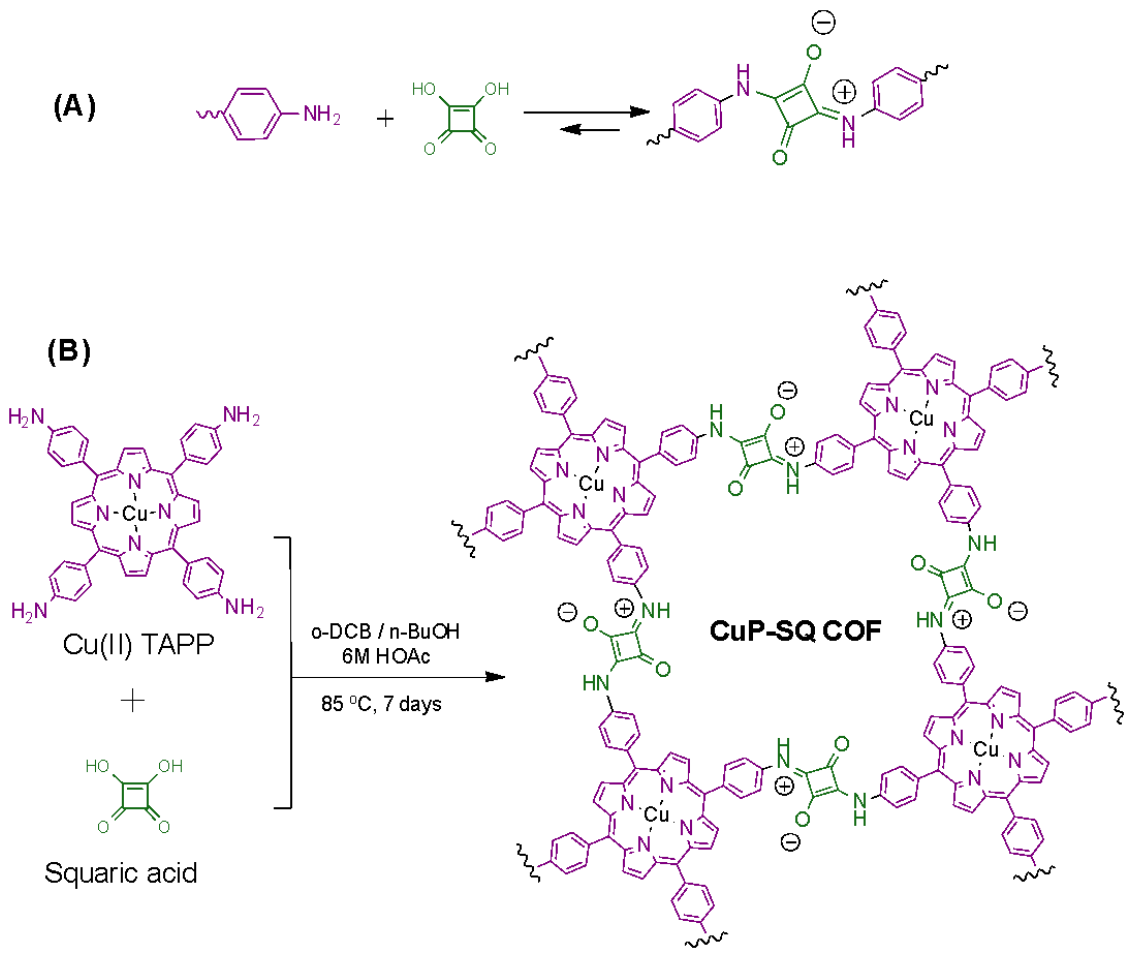
Recently, Fathalla reported the synthesis of new porphyrin COFs through the condensation between TAPP and pyromellitic dianhydride (scheme 10) [16]. Furthermore, the post-synthetic metallation of the free-base porphyrin macrocycles of the resulting COF with either Zn or Mn metals afforded the metallo-porphyrin COF analogues in excellent yields. The metalated analogues showed higher $CO_2$ uptake capabilities compared to the free-base COF. In addition, $Mn^{III}$-COF was found to be an effective catalyst for the selective epoxidation of styrene to the corresponding epoxide.




**Scheme 10**. Synthesis of TAPP and pyromellitic dianhydride based COFs.

## 2.3. Miscellaneous TAPP based COFs.

Even though the imine and imide bond formation are the most common synthetic approaches to construct TAPP-based COFs. There have been other synthetic strategies that were employed to assemble COFs using TAPP building units. For instance, Jiang et al. harnessed squaraine chemistry to assemble a novel COF (CuP-SQ-COF) through the condensation between Cu-TAPP and squaric acid (scheme 11) [17]. The reported COF are highly stable in solvents and has a zigzagged conformation which prevents the side slippage of the layered structure. In addition, it exhibits a very broad rang of light absorption.




**Scheme 10**. Synthesis of CuP-SQ COF.

## 3. Conclusion.

Owing to its potential applications in many fields as well as predictable structures and pore functionality, COFs have gained considerable attention over the past decade. Porphyrin-containing COFs have been relatively well-explored and proven to be attractive materials in terms of stability and promising applications. Specifically, tetra(4-aminophenyl)porphyrin (TAPP) has been one of the most used building units in constructing various COFs. This review summarized the synthetic approaches employed so far to assemble COFs based on TAPP. The amino groups of TAPP rendering it an attractive building unit for the formation of imine- and imide-linked COFs.

## 4. References

[1] R. Liu, K. T. Tan,Y. Gong, Y. Chen, Z. Li, S. Xie, T. He, Z. Lu, H. Yanga and D. Jiang. Covalent organic frameworks: an ideal platform for designing ordered materials and advanced applications. Chem. Soc. Rev. 50 (2021) 120-242.

[2] D. Jiang. Covalent Organic Frameworks: An Amazing Chemistry Platform for Designing Polymers. Chem. 6 (2020) 2461-2483.

[3] K. Geng, T. He, R. Liu, S. Dalapati, K. T. Tan, Z. Li, S. Tao, Y. Gong, Q. Jiang, and D. Jiang. Covalent Organic Frameworks: Design, Synthesis, and Functions. Chem. Rev. 120 (2020) 8814–8933.

[4] H. Furukawakyle, C. O'keeffeand and O. M. Yaghi. The Chemistry and Applications of Metal-Organic Frameworks. Science 341 (2013) 6149.

[5] Q.-Y. Liu, J.-F. Li and J.-W. Wang. Research of covalent organic frame materials based on porphyrin units. J Incl Phenom Macrocycl Chem. 95 (2019) 1–15.

[6] A.P. Côté, I. A. Benin, N. W. Ockwig, M. O'Keeffe, A. J. Matzger and O. M. Yaghi. Porous, crystalline, covalent organic frameworks. Science 310 (2005) 1166–1170.

[7] S. Wan, F. Gándara, A. Asano, H. Furukawa, A. Saeki, S.K. Dey, L. Liao, W.W. Ambrogio, Y.Y. Botros, X. Duan, S. Seki, J.F. Stoddart and O.M. Yaghi. Covalent organic frameworks with high charge carrier mobility, Chem. Mater. 23 (2011) 4094–4097.

[8] S. Kandambeth, D.B. Shinde, M.K. Panda, B. Lukose, T. Heine and R. Banerjee. Enhancement of chemical stability and crystallinity in porphyrin containing covalent organic frameworks by intramolecular hydrogen bonds. Angew. Chem. Int. Ed. 52 (2013) 13052–13056.

[9] B. Gole, V. Stepanenko, S. Rager, M. Grüne, D.D. Medina, T. Bein, F. Würthner and F. Beuerle. Microtubular self-assembly of covalent organic frameworks. Angew. Chem. Int. Ed. 57 (2018) 846–850.

[10] X. Xu, S. Wang, Y. Yue, and N. Huang. Semiconductive Porphyrin-Based Covalent Organic Frameworks for Sensitive Near-Infrared Detection. ACS Appl. Mater. Interfaces 12 (2020) 37427–37434.

[11] Y. Li , J. Zhang, K. Zuo, Z. Li, Y. Wang, H. Hu, C. Zeng, H. Xu, B. Wang and Y. Gao. Covalent Organic Frameworks for Simultaneous $CO_2$ Capture and Selective Catalytic Transformation. Catalysts 11 (2021) 1133.

[12] X. Wu1, X. Zhang, Y. Li, B. Wang, Y. Li and L. Chen. A porphyrin-based covalent organic framework with pH-dependent fluorescence. J. Mater. Sci. 56 (2021) 2717–2724.

[13] R. Shen, W. Zhu, X. Yan, Ta. Li, Yo. Liu, Y. Li, S. Daia and Z.-G. Gu. A porphyrin porous organic polymer with bicatalytic sites for highly efficient one-pot tandem catalysis. Chem. Commun. 55 (2019) 822-825.

[14] V. S. P. K. Neti, J. Wang, S. Deng, and L. Echegoyen. Synthesis of a Polyimide Porous Porphyrin Polymer for Selective CO2 Capture. J. Chem. (2015) Article ID 281616: http://dx.doi.org/10.1155/2015/281616.

[15] C. Zhang, S. Zhang, Y. Yan, F. Xia, A. Huang, and Y. Xian. Highly Fluorescent Polyimide Covalent Organic Nanosheets as Sensing Probes for the Detection of 2,4,6-Trinitrophenol. ACS Appl. Mater. Interfaces 19 (2017) 13415–13421.

[16] M. Fathalla. Synthesis, $CO_2$ Adsorption and Catalytic Properties of Porphyrin-Pyromellitic Dianhydride Based Porous Polymers. Macromol. Res. 29 (2021) 321–326.

[17] A. Nagai, X. Chen, X. Feng, X. Ding, Z. Guo, and D. Jiang. A Squaraine-Linked Mesoporous Covalent Organic Framework. Angew. Chem. 125 (2013) 3858 –3862.

# Silicon nanocrytallines composite sol-gel rod for optical applications

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## Abstract

Nanocrystallines silicon (NCs Si) powders of heterogeneous sizes were uniformly dispersed in some solvents. Different quantity of NCs Si powder (0.00150/0.0012/0.0070) g was taken in the 10 ml of solvents to identify the effect of photoluminescence property. The NCs Si solution was directly incorporated in sol-gel matrix and developed nanocomposite rods. Light emitting from NCs Si solutions and nanocomposite rods were detected by exposing UV light. Optical properties of the NCs Si solution and nanocomposite rod were systematically studied using different characterization techniques. The effect on the properties of NCs Si in the environment of sol-gel matrix was studied. The significant change in absorption and emission property of NCs Si solution is observed when embedded in sol-gel matrix. The predicted band gap 2.8 eV of NCs Si in solution was changed to 3.63 eV when it is included in solid matrix. Crystalline structures of different sizes of NCs Si are identified by XRD and TEM. Well presence and distribution of NCs Si in the sol-gel surface were revealed by SEM images and EDX spectra. Spontaneous emissions (SE) of NCs Si solution and nanocomposite sol-gel rods were tested using third harmonic 355 nm laser source of a pico second tunable laser system. The enhanced SE signal from the nanocomposite solid rod is quite significant, which indicates that SE signal may enable to increase if highly packed NCs Si colloidal solution employ in sol-gel rod. The fabrication of light emitting composite solid rod may use as a solid state active medium for the ASE testing in the future work.

**Keywords**: Nanocrystals silicon, Sol-gel, Absorption, Emission, Spontaneous Emission and pico-second laser source

**قضبان هلام السيليكون النانوية المركبة للتطبيقات البصرية**

**الملخص**: تم تفريق مساحيق السيليكون النانوية ( (NCs Siذات الأحجام غير المتجانسة بشكل موحد في بعض المذيبات. تم أخذ كمية مختلفة من مسحوق NCs (0.0070 / 0.0012 / 0.00150)جم في 10 مل من المذيبات لتحديد تأثير خاصية التلألؤ الضوئي. تم دمج محلول NCs Si مباشرة في مصفوفة sol-gel وتطوير قضبان مركّبة نانوية. تم الكشف عن الضوء المنبعث من محاليل NC وقضبان المركبات النانوية عن طريق تعريض ضوء الأشعة فوق البنفسجية. تمت دراسة الخواص البصرية لمحاليل NCs Si وقضبان المركبات النانوية بشكل منهجي باستخدام تقنيات توصيف مختلفة. تمت دراسة التأثير على خصائص NCs Si في بيئة مصفوفة sol-gel. لوحظ التغيير الكبير في خاصية الامتصاص والانبعاث لمحلول NCs Si عند تضمينه في مصفوفة sol-gel. تم تغيير فجوة النطاق المتوقعة 2.8 فولت من NCs Si في المحلول إلى 3.63 فولت عندما يتم تضمينها في مصفوفة صلبة. يتم تحديد الهياكل البلورية ذات الأحجام المختلفة من NCs Si بواسطة XRD و TEM. تم تأكيد وجود جيد وتوزيع NCs Si في سطح sol-gel بواسطة صور SEM وأطياف EDX. تم فحص الانبعاثات العفوية ( (SEلمحلول NCs Si وقضبان sol-gel المتناهية الصغر باستخدام مصدر ليزر 355 نانومتر التوافقي الثالث لنظام ليزر بيكو قابل للضبط الثاني عالي الطاقة. تعد إشارة SE المحسّنة من قضيب صلب المركب النانوي مهمًا جدًا ، مما يشير إلى أنه قد يكون من الممكن تحسين إشارة SE في المستقبل إذا تم استخدام محلول NCs Si الغرواني المعبأ للغاية في قضبان -sol. gel قد يستخدم تصنيع القضيب الصلب المركب الباعث للضوء كوسيط نشط للحالة الصلبة لاختبار ASE في العمل المستقبلي.

## 1. Introduction

In the past decades, silicon-based nanocrystallines (NCs-Si) /nanoporous (Psi) have been interested for new type of photoelectronic and informational materials. Extensively, bulk silicon has been treated as an incompatible material for optical applications because of its incapable to emit light and indirect band gap in nature [1]. After the detection of luminescent light from nanoporous (Psi) and nanocrystals silicon (NCs-Si) by Canham in 1990 [2], it changed the view on this material for optical devices. For Si integrated circuits [3], the researchers have activated especially in the preparation and characterization the light emitting of Psi and NCs-Si [4]. The emission property of silicon nanoparticles are multi-colors with size dependent, which are considered as potential materials for fluorescent tags, biological imaging and bioanalysis [5-8]. Interestingly, luminescence Psi and NCs-Si are brighter with significant stable to photo bleaching [9], tunable at multi wavelengths than florescent organic dyes [10]. Nanocrystals silicon has nontoxic behavior and attracted for the application in pollution [11].

In fact, the proper use of NCs-Si/Psi in the light emitting applications such as (LEDs or injection lasers) is still interested including for fundamental research as well as for waveguides, photodetectors, solar cells, gas sensors [12 - 14] etc. The main challenge is to achieve ASE or lasing in silicon for optical circuits because the basic component is the laser light source. For the goal, a proper study on the photoluminescence properties of NCs-Si or Psi solutions under different conditions are still required. The good stability of porous silicon with high concentration in solution still is one of the important issues [15]. In this regard, the deposition of NCs Si in an insulator matrix environment, such as SiO2 matrix [16] were performed by physical techniques [17-18] because it can control the influences of the interface between the NCs Si and matrix. In addition, to realize the PL efficiency, fabrication and crystallization of nanocrystal silicon in SiO2 at low percent was performed using high thermal annealing techniques [19, 20]. Efforts have been ensued to increase the emission property of NCs-Si in SiO2 using high thermal annealing process [21–27]. However, the disadvantage of thermal annealing process is considered as incompatible for the addition of LEDs in electronic systems. The higher band

gap of the nanocrystals silicon in SiO2 matrix leads to a drawback when it operates with voltage of LEDs [28]. Therefore, strong emission from silicon nanoparticles with high density and small band gap for the optimization of optoelectronic properties was suggested [29]. To stabilize and maintain the photoluminescence (PL) property in matrix, direct incorporation of silicon nanoparticles in different matrices such as sol-gel derived fine powder [30], sol-gel derived-films [31], composites block silica matrix [32], silica aerogels pellets composites [33], blocks of aerogel [34] and NCs Si in aerogels film [35] were performed.

Indeed, inclusion of silicon nanoparticles in sol-gel matrix is easily controllable and able to combine with high density of nanopart icles in view of desired applications. Optical stability of silicon nanoparticles within the matrix at low temperature may lead to light stimulation, for this, our group have carried out a series of studies on the optical and structural properties of porous silicon in sol gel [36-38], ormosils [39] and polymer matrix [40). In previous, we used to dope the chemically synthesized porous silicon in the matrices which observed significant unstable of particles during the drying of the matrix except the polymer matrix. Preparation of high density colloidal porous silicon based solution by chemical etching route is a major issue [15]. On other hand, we doped commercially obtain nanocrystal silicon powder in sol-gel hosts [41-42]. Results revealed that observed optical property of silicon nanocrystalline powder was significantly stable as compared to porous silicon in sol gel matrix during aging. In the present study, commercially obtained nanocrystalines Si powder were dispersed in some solvents and prepared colloidal solutions. Emission light from NCs Si solutions was tested under UV lamp before use. The light emitting solution was doped in sol-gel matrix and investigated by different characterization techniques. Spontaneous emissions of solution and composite samples were examined using a laser source of pico second laser system. The obtained properties of silicon monocrystalline composite sol gel are systematically discussed.

## 2. Materials and Preparation method

The nanocrysts silicon powder was procured from M K Impex, Canada (98+% -pure), heterogeneous size range (APS: 5-25nm). The NCs powder was prepared as a colloidal solution. For colloidal solution, the different approximate concentration of NCs Si powder was taken and dispersed in known volume of different solvents, such as ethanol, methanol, ethyl acetate, DMSO, acetone, DMF, acetonitrile, and formamide. The solutions were ultra-sonicated for well dispersion and centrifuged to remove the residue particles. Then the solutions were exposed to an UV lamp (Cole-Parmer, USA) of 365 nm to detect the light emitting.

The NCs Si composite material was prepared using sol-gel technique. In the process, the inorganic precursor TEOS (Si $(OC_2H_5)_4$) (Aldrich, 98%) was taken as the starting material and reacted with ethanol (Riedel-deHaen) for hydrolysis and polycondensation to make sols. In composition, about 15-20 ml of TEOS was mixed with 20-25 ml of ethanol and stirred about 25-30 min. Then, about 10 ml of formamide as DCCA was included into the solution. The mixed solution was continously stirred for another 15 min. After dropping of 1 ml nitric acid as catalyst in 15 ml of distilled water, it poured drop wise in solution and stirred about 10-15 minutes. The NCs Si of 0.00150 g concentration based formamide solution was directly added in the final sol. The final composite sol was separated in some polystyrene tubes and cuvettes for drying at room temperature. Before aging, composite sol in tubes and quartz was sonicated to insure a homogenous distribution of particles. The nanocomposite sol becomes a gel in the tube and cuvette cell after a few weeks. The gel samples were transformed into solid state rod in the polystyrene tube after 4-5 weeks. The composite containing tube was preserved at 55$^{o}$C in an oven for few days to vaporize the liquid. The final product rod was performed cutting and hand polishing for PL and SE test by laser action.

## 3. Characterization

The optical, structural, and SE properties of nanocrystals silicon in solvents and sol gel were investigated. The different properties of the NCs Si samples were recorded at room temperature.

X-ray diffraction (XRD) spectra of the NCs Si powder were scanned using a PANalytical X'Pert X-ray diffractometer. Absorption and
emission were recorded in UV-visible-NIR spectrophotometer (Jasco 670) and Fluorescence Spectrophometer (Lumina Thermo) respectively. The morphological structure of the NCs Si in solvent and in sol-gel matrix was examined by a field emission scanning electron microscope (FESEM, JEOL, JSM-6380LA). Particle size of NCs Si in the solution and matrix at high resolution were determined by transmission electron microscopy (JEOL, JEM2100F). The spontaneous emission spectra were examined using laser source of Pico Second Tunable Laser System (Lotti III) and monitored with ICCD Spectrograph (Andor).

## 4. Results and discussion

The crystalline structure of NCs-Si powder was inspected by XRD. The XRD data shows the original pattern of NCs-Si powder. The pattern of the NCs Si is found to be a good correspond to peak position and relative intensity of the standard pattern, indicating the high purity of Si powder. The observed peaks at 28.41, 47.26, and 56.06 correspond to the crystal plane (111), (220), and (311), respectively, as shown in Figure 1.

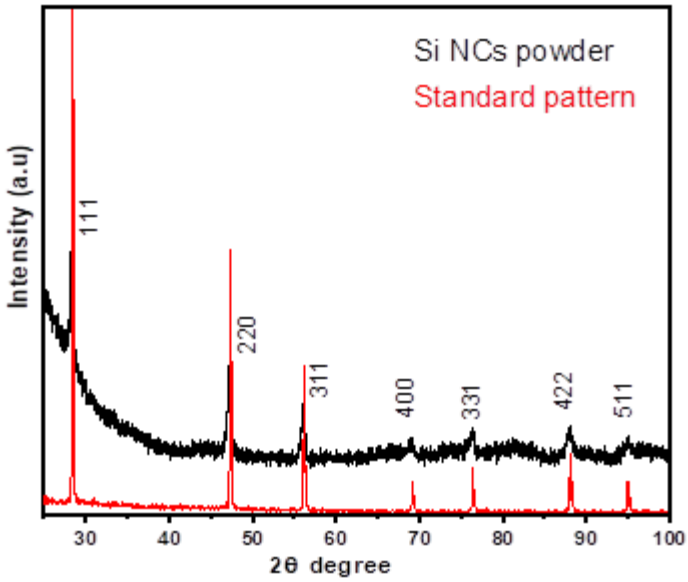


Figure 1: X-Ray diffraction pattern of NCs Si powder

Different concentration of the NCs silicon powder was used in various solvents. The solvents were selected as some polar and nonpolar which are ethanol,

methanol, ethyl acetate, acetonitrile, Acetone, formamide, DMSO, DMF, THF, dioxane. Some NCs Si solutions were detected the emission light under the exposure of UV lamp. The NCs Si containing formamide, DMF, and DMSO solutions were found to be good luminescent under the naked eye of UV lamp. No luminescent light was detected from the NCs Si in THF, dioxane, ethanol, methanol, ethyl acetate, and acetonitrile acetone, which are not discussed in this work. The luminescent and non-luminescent light from NCs Si in different solvents is listed in Table 1. In addition, the NCs dispersed ethanol, methanol, ethyl acetate, acetonitrile, acetone, THF, and dioxane solution were aggregated or precipitated. The digital image of luminescent NCs Si in solvents is shown in Figure 2.

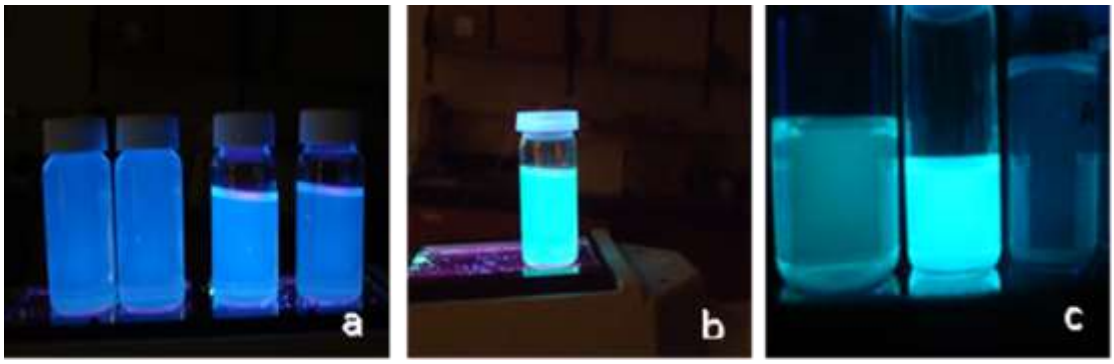


Figure 2: The digital image of light emitting NCs Si in:
(a) Formamide, (b) DMF, (c) DMSO solvent under UV exposure

Table 1: Details of NCs silicon in different solvents

| Solvents | Nanocrystallines powder solution | PL | Stability |
|---|---|---|---|
| Ethanol | NCs Si | No | Aggregate |
| Methanol | NCs Si | No | Aggregate |
| Water | NCs Si | No | Aggregate |
| Formamide | NCs Si | Yes | Stable |
| N,N-DMF | NCs Si | Yes | Stable |
| DMSO | NCs Si | Yes | Stable |
| Ethyl acetate | NCs Si | No | Dispersed |
| Acetonitrile | NCs Si | No | Dispersed |
| Acetone | NCs Si | No | Precipitate |
| Dioxane | NCs Si | No | Precipitate |
| THF | NCs Si | No | Dispersed |

The light emitting from NCs silicon in some solvents is detected under the exposure of UV lamp. Thus, the formamide based solution was selected to study the different properties of the NCs Si using different characterization techniques. The property of light emitting NCs Si dispersed DMSO, and DMF solution is not detailed except the images as shown in Figure 2. The NCs Si dispersed formamide solution was then incorporated in sol-gel matrix and developed into nanocomposite rod in order to examine the stimulated emission spectra under tunable laser system. The crack free composite rods were successfully prepared. It was easily able to cut and hand polished without any harmful to dopant. After cutting and polished, the nanocomposite rod was used to investigate the different properties. The digital image of the light emitting polished rod with and without UV exposure is seen in Figure 3 (c, d). The light emitting nanocomposite rods with the evolution of sol to solid rod under UV exposure is displayed in Figure 3 (a). The emitting color indicates the well dispersal and existence of NCs Si in the matrix environment.

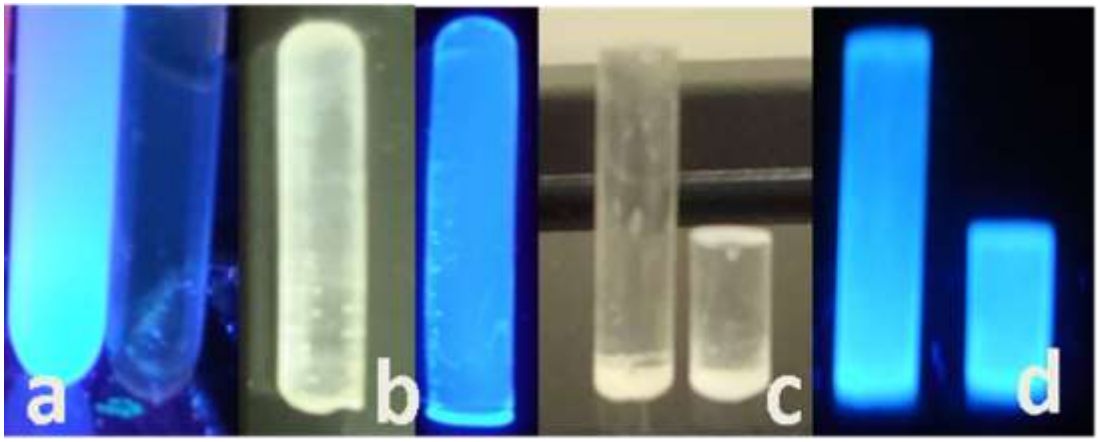


Figure 3: The digital image of NCs Si doped (a) sol (b) rods before cutting (c) rod after cutting and (d) rods under UV light exposure.

As clearly seen in figure 3 (b), the digital image of light emitting nanocomposite rod which is comparable to the solution one. Brightness of nanocomposite rods indicates the significant stable of the NCs Si in sol-gel solid environment.

### 4.1. Morphology and Size

Morphological structure of NCs Si in solvent and composite matrix was inspected by SEM at high magnification scale is shown in Figure 4 (i). The native of nanocrystallines silicon in solvent is quite identical and closely

gathered in the surface and similar to sandy surface. When NCs Si in the dried sol-gel surface, the nanoparticles become mono distribution in the micro-amorphous matrix environment as seen in Figure 4 (ii). The structure of NCs Si in the dried sol gel indicates the particles lie in the homogenous amorphous surface of matrix. Additionally, the role of DCCA in sol-gel composition can control stressing in sol-gel surface during drying and aging. Involvement of formamide as DCCA in matrix may help to form crack free structure. This may reason to the well distribution of NCs Si and stable provide good formidable rods. In general, dopant particles are sometimes evaporated during the transition phase of sol gel drying process, but the use of DCCA in the process may slow down the evaporation of NCs Si. Therefore, NCs Si doped sol-gel rod were found to be more stable than the porous silicon (Psi) doped sol-gel rod [15, 38-39].

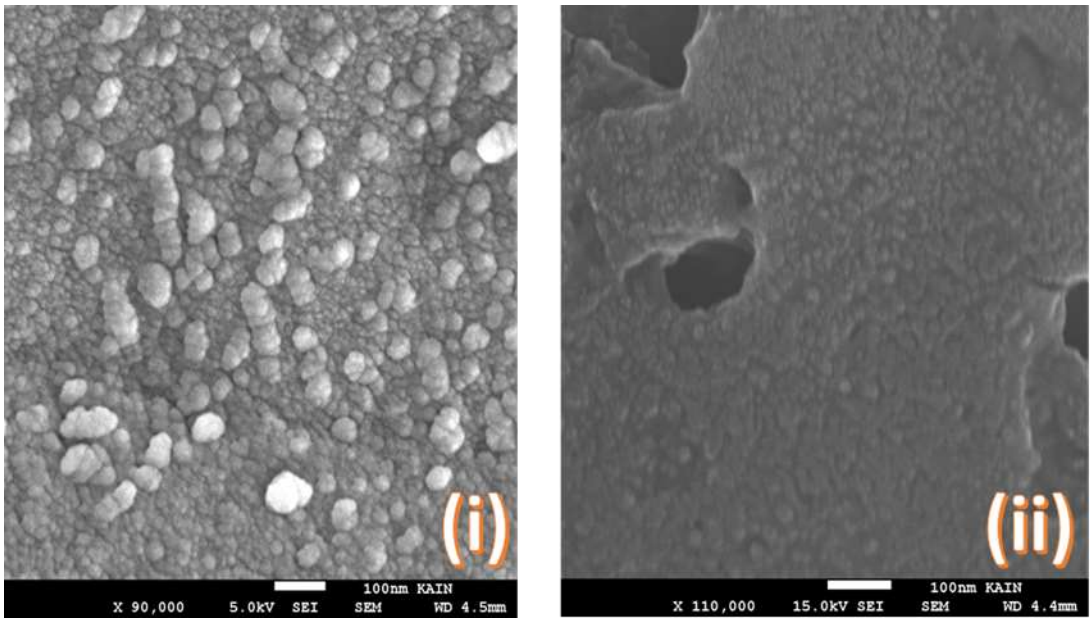


**Figure** 4. The SEM images of NCs Si in (i) solution and (ii) sol-gel matrix

Figure 5 (i) shows the typical TEM images for NCs Si solution at low and high resolution. Distribution of mono dark spot Si particles in the solvent is observed. Crystalline lattice structure of NCs Si particles about 3-7 nm size were detected as shown 5 (i-inset). Majority of Si particles are spherical with diameters ranging from 5 nm to 8 nm with highly crystalline in nature. NCs Si are distributed in sol-gel matrix with a roughly spherical shape as seen in Figure 5 (ii). The sizes of NCs Si are larger due to the envelope of sol-gel surface. Well presence of NCs Si in the solution is detected by EDX spectra as seen in Figure

5 (iii). The existence of NCs Si in the matrix is confirmed by EDX spectra as shown in Figure 5 (iv). Significant presence of NCs Si particles inside the surface of the matrix environment is witnessed by the image and EDX spectra which lead to enhance substantial strong emission light under UV light as shown in Figure 3.

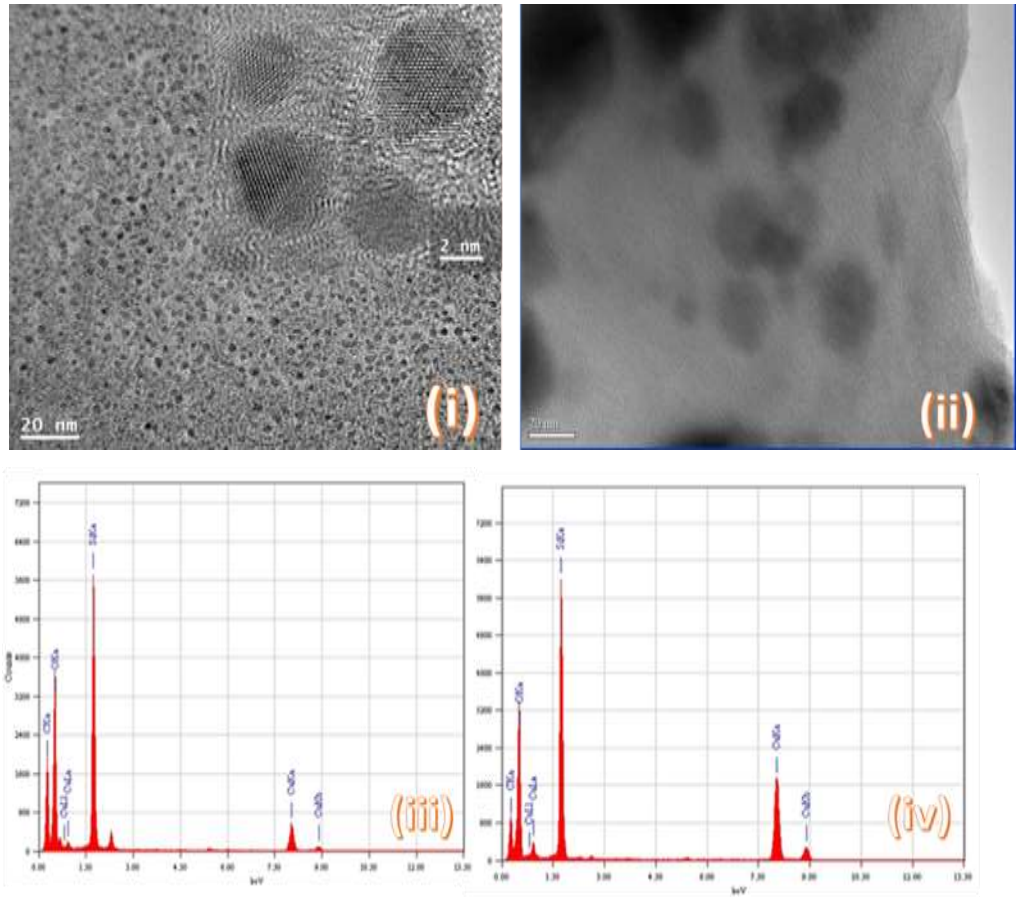


Figure 5. The TEM images of NCs Si in (i) solution at low and high resolution (inset) (ii) sol-gel matrix (iii) EDX of solution and (iv) EDX of nanocomposite

### 4.2. Absorption property

The absorption spectra of NCs Si in formamide at different concentration was measured. The absorbance is exponentially increased when the concentration increases in solution. There is no effect of the relative peak position relative to the concentration of NCs. The absorption spectra of NCs Si colloidal solution at different concentration are compared as shown in Figure 6 (i). Absorption spectra of NCs Si composite sol-gel matrix was recorded in the same spectral region. The absorbance and peaks of NCs Si in sol-gel are changed with broadening bandwidth. Shifting of peak and broadening the relative bandwidth may attribute to the solid environment of the matrix as listed data in Table 2.

Relative absorption peaks at 290 nm and 356 nm are observed in solution. The corresponding absorption peak of NCs Si are slightly shifted in sol-gel matrix as shown in Figure 6 (ii), the peaks 'a' and 'b'. The absorbance of the two peaks slightly increased in the sol gel. The comparison peaks of NCs Si in sol gel and solution are shown in Figure 6 (ii), a, b, c, and d peaks respectively.

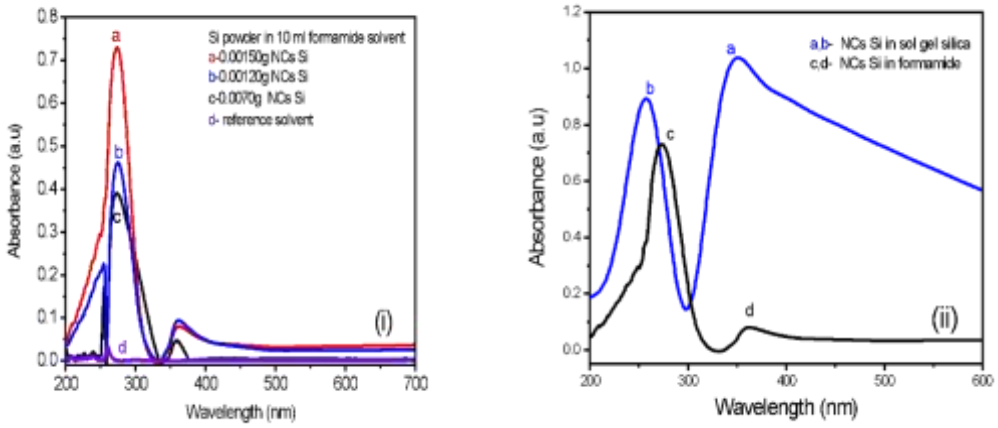


Figure 6. Absorption spectra of NCs Si (i) solution at different concentration (ii) comparison with composite sol-gel matrix

### 4.2. Energy band gap

To examine the energy band gap of the NCs Si, the coefficient (α) was deduced from the absorption spectra using the relation

$$\alpha = 2.303 \frac{A}{d}$$

Where the parameter d and A are the thickness and the optical absorbance of the film.

The band gap of the NCs Si in solution and sol gel was calculated from Tauc's plots [43] by explaining the relationship between coefficient (α) and photon energy for indirect band transition

$$(\alpha h\nu) = C(h\nu - E_g)^n$$

Where the parameters hν, C and $E_g$ are the photon energy, a constant and the optical band gap respectively. The 'n' is a dependence parameter on the band of direct or indirect transition and the property of electron density in the valence and conduction bands.

The parameter $(\alpha h\nu)^{1/n}$ was plotted with photon energy for different values of n. But, for the direct allowed transition, best fit was found when n = 2, whereas

n=1/2 for an indirectly allowed transition. Such result indicates that the indirect transition behavior of noncrystalline materials. From the Tauc's equation for the allowed nondirect transition, the $E_g^{opt}$ (optical band gap) values can be obtained from the intercept of $(\alpha h\nu)^{1/2}$ vs $(h\nu)$ when $(\alpha h\nu)^{1/2} = 0$.

The calculated band gap of NCs Si in formamide is shown in Figure 7(i). However, the band gap slightly changes from 2.9 eV of solution to 3.62eV in sol gel as displayed in Figure 7 (ii). The change in bandgap of NCs Si is due to the solid environment of matrix. The values of band gap for each NCs Si sample is detailed in **Table. 2.** Therefore, the optical band gap of NCs Si may depend on the physical environment of matrix and size.

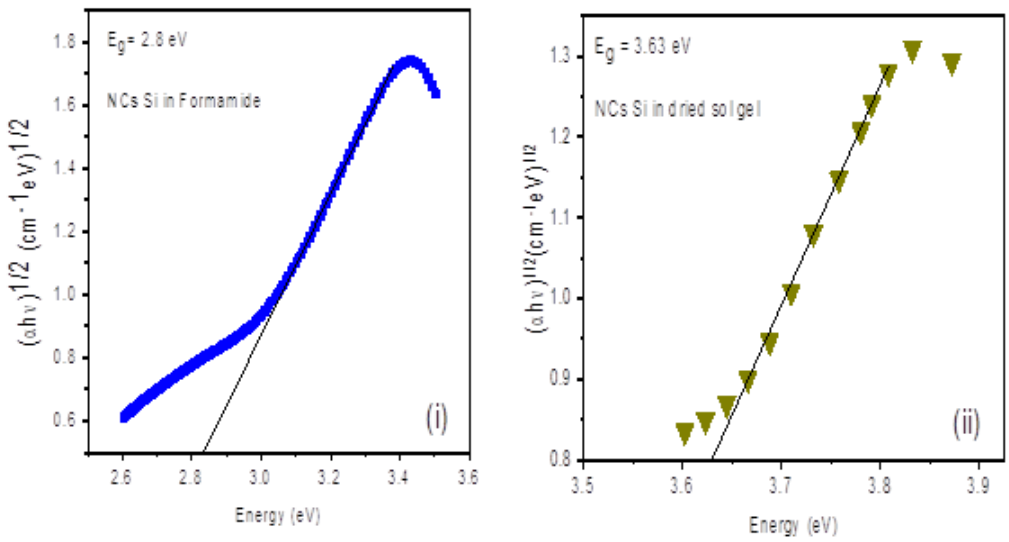


Figure 7. Optical band of NCs Si in (i) formamide (ii) sol-gel matrix

**Table 2**: Detail of different properties of NCs Si in solution and sol gel matrix

| Sample | Energy band gap (Eg) | Absorption peak positions | Emission peak positions | Excitation peak positions | Spontaneous emission peak positions |
|---|---|---|---|---|---|
| NCs Si in formamide | 2.8 eV | 275 nm<br>360 nm | $a_1$, $b_1$-442 nm | $a_2$, $b_2$-365 nm | 435 nm |
| NCs Si in dried sol gel | 3.63 eV | 350 nm<br>257 nm | $a_1$, $b_1$-440 nm | $a_2$, $b_2$-366 nm | 429 nm |

## 4.3. Photoluminescence and spontaneous emission property

From the points of application, the photoluminescence (PL) mechanism of silicon nanoparticles in solid media was recorded and compared with the spectra of NCs Si solution. The excitation wavelength was selected as that exhibited the intense emission spectra and within the range of the absorption spectra of the NCs Si solution. The selected excitation wavelength was taken as an excitation pump laser source. For emission spectra, the sample was measured at different excitation wavelength to examine the intense emission peaks. Figure. 8 shows the emission and excitation spectra of NCs Si in formamide solvent and sol-gel matrix. It shows that the intense emission intensity was not observed at the excitation wavelength correspond to the strong absorbance peak of the NCs Si.

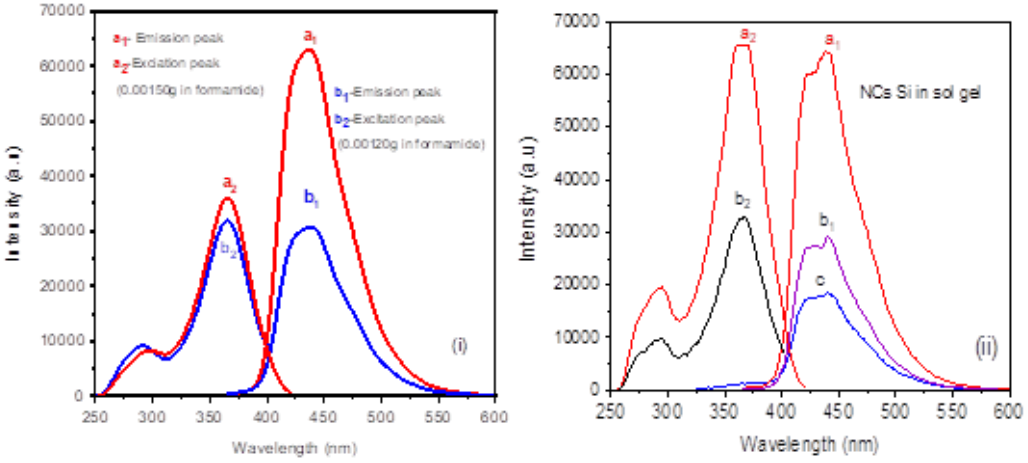


Figure 8. Emission and excitation spectra of NCs Si in (i) solution (ii) sol-gel matrix

Significantly influence on the emission and excitation intensity is observed due to different concentration of NCs Si in solution. Higher concentration of NCs Si in solution is pronounced the stronger intensity as appeared at the emission peaks ($a_1$, $b_1$-442 nm) and excitation peaks ($a_2$, $b_2$-365 nm) as shown in Figure 8 (i). No major effect with peak position upon the variation of concentration is observed. The intensity of emission and excitation peaks of NCs Si solution are influenced when it included in the matrix environment. The emission and excitation spectra of NCs Si in solid sol-gel were recorded using different excitation wavelengths 365 nm, 355 nm, and 315 nm as shown in Figure 8(ii). The emission peak is substantially stronger at excitation of 365 nm than the excitation of 355 nm and 315 nm. For instance, the peaks $a_1$, $b_1$, and c are the emission of NCs Si in the sol gel at excitation of 365 nm, 355 nm, and 315 nm respectively as displayed in Figure 8 (ii). The excitation peak position of different solution observed at around 365 nm ($a_2$ and $b_2$) do not change as shown Figure 8 (i) and listed in Table 2. It means that stability of NCs Si in sol-gel environment during drying is much better than the porous silicon in sol-gel as our previously reported [36-37]. The emission intensity of NCs Si in sol gel matrix is quite significant as compared to intensity of NCs Si solution which may attribute to influence of temperature of sol gel $SiO_2$ environment during aging since the improvement in PL intensity of NCs Si in $SiO_2$ upon annealing temperature was observed [44]

The spontaneous emission (SE) from the NCs Si composite sol gel rod was examined by employing a 355nm pico second laser source. But intense emission of NCs Si in sol gel rod was attained at excitation of 365 nm as displayed in 8 (ii). Observation of NCs Si solution and composite sol-gel rod were conducted at the same condition under a high power tunable pico second laser source. The SE spectra of NCs Si solution were recorded at two concentrations. The NCs Si solution and composite rod were pumped at 3 mj, 6 mj and 10 mj laser energy as shown in Figure 9 (i-ii). There is exponentially increased in relative intensity with respect to concentration and pump energy. For instance, the observed SE intensity at 3 mj is weaker than the relative intensity of 6 mj as seen in Figure 9 (iii). It indicates that the luminescent intensity of the NCs Si depends on the pump energy. When the excitation energy increased at 10 mj, SE intensity of NCs Si solution is improved as shown

in Figure 9 (iv). The behavior of SE intensity for NCs Si solution depends on the proper pump energy with the concentration. The SE stability of NCs Si in formamide is quite significant and more superior than the porous silicon in THF and dioxane under laser action [38-39].

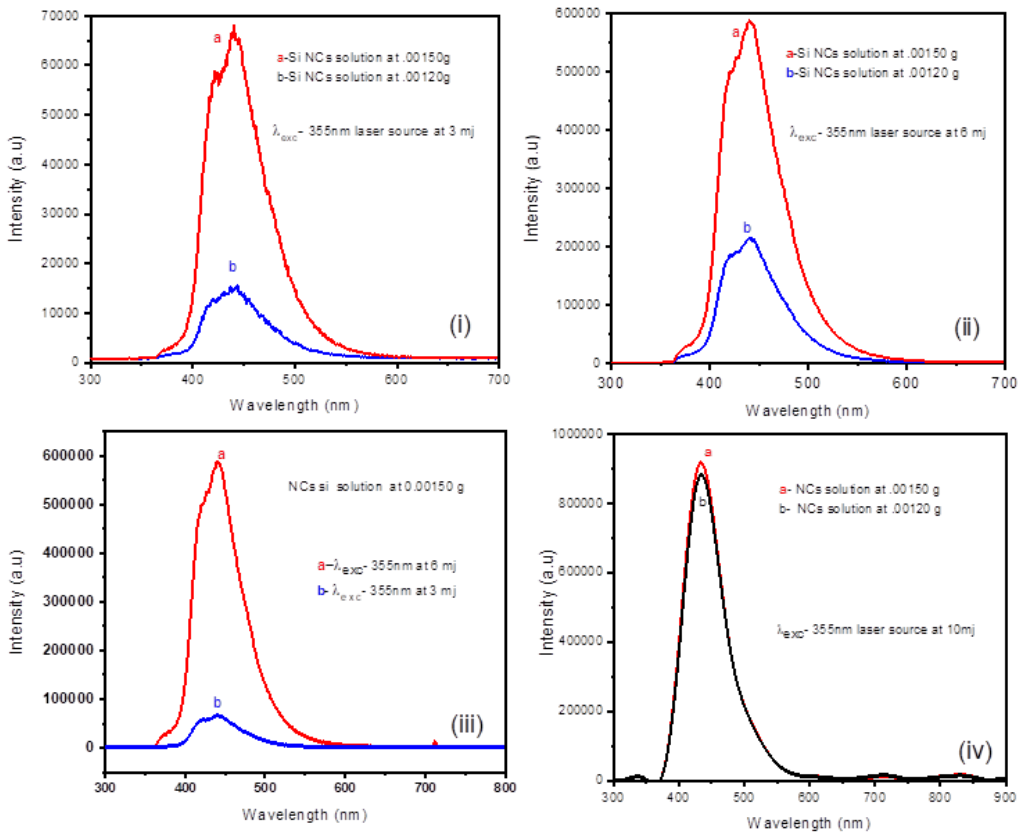


Figure 9. Spontaneous emission spectra of NCs Si in (i-iv) solution at different concentration and pumped energy

Therefore, influence on spontaneous intensity of NCs Si solution is the factor of concentration, excitation wavelength, and pump energy. As clearly indicate that the exhibited light from NCs Si solution is about 5 times intense when the pump intensity increases from 3 mj to 6 mj and 10 mj is shown in Figure 9 (iii-iv).

For NCs Si composite rod, SE spectra were recorded at the same condition as NCs Si solution. The enhanced SE spectra of composite rod are quite significant as a compare to solution. The SE intensity of NCs Si in solid matrix environment at different pump energy is significantly improved as shown in Figure 10 (i).

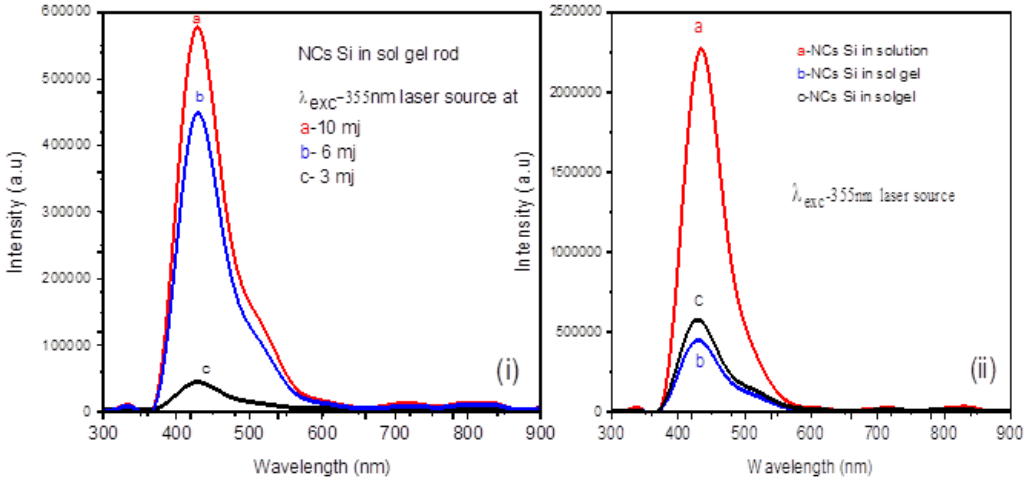


Figure 10. Spontaneous emission spectra of NCs silicon doped sol gel (i) rod (ii) comparison solution and rod

The influence of SE intensity upon increasing pump energy from 3 mj to 10 mj is observed. When the nanocomposite rod is excited at 3mj, the intensity is quite low, but it increases dramatically at the excitation of 6mj as seen at the peaks 'b' and 'c' in Figure 10(i). Intensity is further increasing as the pump energy increases at 10 mj. No major effect at peak positions is observed upon changing the pump energy. Comparison of SE between composite sol gel and solution indicates the slightly effect on peak position. The SE peak of NCs Si in sol-gel matrix changes roughly about 10 nm from solution which is attributable to the effect of solid environment as shown in figure 10 (ii). In figure 10 (ii), the peak 'a' of NCs Si solution is slightly shifted when it is in sol-gel matrix i.e. the peaks 'b' and 'c'. Well distribution and stability of NCs Si in solid matrix environment lead to good enhancement of SE in comparison to the porous silicon solution based composite sol-gel matrix as reported in [15, 36-39]. Therefore, the obtained SE spectra of the NCs Si composite rod revealed that NCs Si are well dispersed in the matrix without aggregation. It may possible to embed high concentration of NCs Si based solution in sol-gel matrix for SE improvement that can further lead to ASE.

## Conclusion

In the present work, NCs solution was prepared using NCs Si powder. The NCs Si solution was directly included in sol prepared by sol-gel technique. The NCs Si composite sol gel was further solidified to develop into rod and characterized by using different optical techniques. Well distribution and presence of NCs Si in the matrix environment were confirmed by SEM and EDX spectra, respectively. The optical properties of the composites rod are shown to be significantly stable. Photoluminescence property of NCs Si is quite enhanced in sol-gel media. Influence at peaks of NCs Si in the matrix is observed due to the solid environment. The significant spontaneous emission of the composite rod is obtained and influenced by pump energy. It may conclude that NCs silicon-based solution may directly include and stabilize in sol-gel matrix which is able to transform into a composite rod to test the stimulated emission under laser system.

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## References

[1] S. Hayashi, K. Yamamoto, Optical properties of Si-rich SiO2 films in relation with embedded Si mesoscopic particles, J Lumin, 70, 352-363, 1996.

[2] L. T. Canham, Silicon quantum wire array fabrication by electrochemical and chemical dissolution of wafers, Appl. Phys. Let, 57, 1046, 1990.

[3] B. S. Kim, D. I. Kim, C. W. Lee, Photoluminescence from nano silicon materials prepared by photoelectro chemical methods, J. Korean. Phys. Soc., 38, 245, 2001.

[4] U. Gosele, V. Lehmann, Light emitting porous silicon, Mater. Chem. Phys, 40, 253, 1995.

[5] W. C. Chan, S. Nie, Quantum dot bioconjugates for ultrasensitive non-isotopic detection, Science, 281, 2016, 1998.

[6] M. Bruchez, Jr. M. Moronne, P. Gin, S. Weiss, A. P. Alivisatos, Semiconductor nanocrystals as fluorescent biological labels, Science, 281, 2013, 1998.

[7] T. D. Lacoste, X. Michalet, F. Pinaud, D. Chemla, A. P. Alivisatos, S. Weiss, Ultrahigh resolution multicolor colocalization of single fluorescent probes, Proc. Natl. Acad. Sci. 97, 9461, 2000.

[8] X. Michalet, F. F. Pinaud, L. A. Bentolia, J. M. Tsay, S. Doose, J. J. Li, G. Sundaresan, A. M. Wu, S. S. Gambhir, S. Weiss, Quantum dots for live cells, in vivo imaging, and Diagnostics, Science, 307, 538, 2005.

[9] J. K. Jaiswal, S. M. Simon, Potentials and pitfalls of fluorescent quantum dots for biological Imaging, Trends Cell Biology, 14, 49, 2004.

[10] M. N. Khan, A. S. Al Dwayyan, Influence of solvent on the physical and lasing properties of dye- doped sol gel host, J. Lumin. 128, 1767, 2008.

[11] S. Yang, W. Cai, G. Liu, H. Zeng, P. Liu, Optical study of redox behavior of silicon induced by laser ablation in liquid, J. Phys. Chem. *C,* 113, 6480, 2009.

[12] V. Parkhutic, Porous silicon mechanisms of growth and applications, Solid State Electron, 43, 1121, 1999.

[13] D. Dimova-Malinovska, Application of stain-etched porous silicon in light emitting diodes and solar cells, J. Lumin, 80, 352, 1999.

[14] A. W. Fang, R. Jones, H. Park, O. Cohen, M. Paniccia, J. E. Bowers, Integrated
AlGaInAs-silicon evanescent race track laser and photodetector, *Opt. Express,* 15, 2315, 2007.

[15] M. N. Khan, M.M. A Khan, A.S. Al Dwayyan, J.P. Labis, Comparative Study on Electronic, Emission, Spontaneous Property of Porous Silicon in Different Solvents, J. Nanomater. Article ID 682571, 2014.

[16] L. Pavesi, Routes towards a silicon-based laser, Mater. Today, 8, 18, 2005.

[17] Lalic N, J. Linnros, Light emitting diode structure based on Si nanocrystals formed by implantation into thermal oxide, J. Lumin. 80, 263, 1998.

[18] R. J. Walters, G. I. Bourianoff, H. A. Atwater, Field-effect electroluminescence in silicon nanocrystals, Nat. Mater, 4, 143, 2005.

[19] Z.X. Ma, X.B. Liao, W.C. Cheng, G.Z. Yue, Y.Q. Wang, G.L. Kong, Annealing behaviors of photoluminescence from SiOx:H, J. Appl. Phys. 83, 7934, 1998.

[20] Y.Q. Wang, G.L. Kong, W.D. Chen, H.W. Diao, C.Y. Chen, S.B. Zhang, X.B. Liao, Getting high-efficiency photoluminescence from Si nanocrystals in $SiO_2$ matrix, Appl. Phys. Lett. 81, 4174, 2002.

[21] T. Shimizu-Iwayama, K. Fujita, S. Nakao, K. Saitoh, T. Fujita, Visible photolumi- nescence in Si+implanted silica glass, J. Appl. Phys. 75, 7779, 1994.

[22] N. Lalic, J. Linnros, Light emitting diode structure based on Si nanocrystals formed by implantation into thermal oxide, J. Lumin, 80, 263, 1999.

[23] J.G. Zhu, C.W. White, J.D. Budai, S.P. Withrow, Y. Chen, Growth of Ge, Si, and SiGe nanocrystals in $SiO_2$ matrices, J. Appl. Phys. Vol. 78, 4386, 1995.

[24] V. Vinciguerra, G. Franzò, F. Priolo, F. Iacona, C. Spinella, Quantum confinement and recombination dynamics in silicon nanocrystals embedded in $Si/SiO_2$ super- lattices, J. Appl. Phys. 87, 8165, 2000.

[25] F. Gourbilleau, X. Portier, C. Ternon, P. Voivenel, R. Madelon, R. Rizk, Si-rich/$SiO_2$ nanostructured multilayers by reactive magnetron sputtering, Appl. Phys. Lett. 78, 3058, 2001.

[26] E. Werwa, A. A. Seraphin, L.A. Chiu, C. Zhou, K.D. Kolenbrander, Synthesis and processing of silicon nanocrystallites using a pulsed laser ablation supersonic expansion method, Appl. Phys. Lett. 64, 1821, 1994.

[27] R.J. Walters, G.I. Bourianoff, H.A. Atwater, Field e ff ect electroluminescence in silicon nanocrystals, Nat. Mater. 4. 143, 2005.

[28] G. Franz, A. Irrera, E.C. Moreira, M. Miritello, F. Iacona, D. Sanfilippo, G. Di Stefano, P.G. Fallica, F. Priolo, Electroluminescence of silicon nanocrystals in MOS structures, Appl. Phys. A: Mater. Sci. Process. A74, 1, 2002.

[29] Y.Q. Wang, Y.G. Wang, L. Cao, Z.X. Cao, High-efficiency visible photoluminescence from amorphous silicon nanoparticles embedded in silicon nitride, Appl. Phys. Lett. 83, 3474, 2003.

[30] L. Zhang, J.L. Coffer, T.W. Zerda, Properties of luminescent Si nanoparticles in sol gel matrices, J. Sol-Gel Sci. Technol. 11, 267–272, 1998.

[31] V. Svrcek, I. Pelant, J. L. Rehspringer, P. Gilliot, D. Ohlmann, O. Cregut, B. Honerlage, T. Chvojka, J. Valenta, Dian photoluminescence properties of sol–gel derived SiO layers doped with porous silicon, Mater. Sci. Eng. *C*, 19, 233–236, 2002.

[32] Y. Posada, L.S. Miguel, O. Resto, S.Z. Weisz, C.H. Kim, J. Shinar, Optical properties of nanocrystalline silicon within silica gel monoliths, J. Appl. Phys. 96, 2240, 2004.

[33] A.Y. Karlash, Y.E. Zakharko, V.A. Skryshevsky, A.I. Tsiganova, G.V. Kuznetsov, Photoluminescence properties of silica aerogel/porous silicon nanocomposites, J. Phys. D: Appl. Phys. 43, 335, 2010.

[34] J. Amonkosolpan, D. Wolverson, B. Goller, S. Polisski, D. Kovalev, M. Rollings, D.W.G.M. Grogan, T.A. Birks, Porous silicon nanocrystals in a silica aero gel matrix, Nanoscale Res. Lett. 7, 397, 2012.

[35] E. Borsella, M. Falconieri, S. Botti, S. Martelli, F. Bignoli, L. Costa, S. Grandi, L. Sangaletti, B. Allieri, L. Depero, Optical and morphological characterization of Si nanocrystals/silica composites prepared by sol–gel processing, Mater. Sci. Eng, B79, 55, 2001.

[36] A. S. Al Dwayyan, M. N. Khan, M. S. Al Salhi, Optical Characterization of Chemically Etched Nanoporous Silicon Embedded in Sol Gel Matrix, J. Nanomater, 2012, Articles ID 713203, 2012.

[37] M. N. Khan, A. S. Al Dwayyan, M. S. Al Hossain, Morphology and Optical Properties of a Porous Silicon-Doped Sol-Gel Host, Electron. Mater. Lett, 9, 697-703, 2013.

[38] M. N. Khan, A. Aldalbahi, A. alMohammedi, Investigation of Different Colloidal Porous Silicon Solutions and Their Composite Solid Matrix Rods by Optical Techniques, Journal of ELECTRONIC MATERIALS, 47, 3596, 2018.

[39] M. N. Khan, A. Aldalbahi, A. S. Al Dwayyan, Composite rods based on nanoscale porous silicon in sol–gel silica and ormosil matrices for light-emitting applications, J Sol-Gel Sci Technol, 82, 551–562, 2017.

[40] M. N. Khan, A.S. Al Dwayyan, A. Aldalbahi, Light emitting composite rods based on porous silicon in ormosils and polymer matrices for optical applications, Optics & Laser Technology, 9, 203–211, 2017.

[41] M.N. Khan, A. S. Al Dwayyan, M. S. Al Salhi, M. Al Hoshan, Study on characteristics of silicon nanocrystals. within sol–gel host, J Expt. Nanosci., 7, 120, 2012.

[42] M. N. Khan, A. S. Al Dwayyan, Influence on structural and PL property of nanocrystals silicon doped sol gel matrix, J Optoelectron Adv Mat, 14, 448, 2012.

[43] M. A. Khan, S. Kumar, M. N. Khan, M. Ahamed, A. S. Al Dwayyan, Microstructure and blueshift in optical band gap of nanocrystalline $Al_xZn_{1-x}O$ thin, J. Lumin., 155, 275, 2014.

[44] W. Z Yong, L. K. Xin, R. X Tang, Relative enhancement of photoluminescence intensity of passivated silicon nanocrystals in silicon dioxide matrix, Chin. Phy. B, 21, 9, 097804, 2012.

# Therapeutic uses of Nigella Sativa: a wonder seed

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## Abstract

Owing to its unique results and minimal harmful properties, herbal medicines are recently generating a lot of interest across the world in the therapy of several ailments. Nigella sativa is a popular medicinal herb used all over the world. The abundance of bioactive components, particularly thymoquinone, thymol, α hederin and their antioxidant properties for other potential health benefits is credited with Nigella sativa's pharmacological activities. Previous studies exhibited that Nigella sativa has various potential therapeutic and natural activities like antidiabetic, anti-inflammation, antimicrobial, anticancer, antibacterial, antifungal, antihypertensive, wound therapeutic influences, renal protective and antioxidant properties besides its various other potential health benefits. In conclusion, our findings have enhanced the medical, pharmacological, cultural value, and healing practices of N. sativa, which perhaps aid researchers in approaching the utility, efficacy, and effectiveness of this herb. However, the incorporation of these plants in development and creation of new medications for treating several diseases has not yet been fully exploited. Hereby, this review provides a detailed survey on the scientific literature regarding pharmacological properties, chemical constituents and biological influences of the seeds of this herb.

**Key words:** Nigella sativa, appearance, structural, medicinal value, toxicities.

**الاستخدامات العلاجية لحبة البركة: بذرة عجيبة**

**الملخص:** نظرًا لنتائجها الفريدة والحد الأدنى من الخصائص الضارة ، تولد الأدوية العشبية مؤخرًا الكثير من الاهتمام في جميع أنحاء العالم في علاج العديد من الأمراض. حبة البركة هي عشب طبي مشهور يستخدم في جميع أنحاء العالم. إن وفرة المكونات النشطة بيولوجيًا ، وخاصة ثيموكينون ، ثيمول ، ألفا هيديرين وخصائصها المضادة للأكسدة لفوائد صحية محتملة أخرى تُنسب إلى الأنشطة الدوائية لـ Nigella sativa. أظهرت الدراسات السابقة أن حبة البركة لها العديد من الأنشطة العلاجية والطبيعية المحتملة مثل مضادات السكر ، ومضادة للالتهابات ، ومضادات الميكروبات ، ومضادات السرطان ، ومضادات الجراثيم ، ومضادات الفطريات ، ومضادة لارتفاع ضغط الدم ، والتأثيرات العلاجية للجروح ، وخصائص الحماية الكلوية ومضادات الأكسدة إلى جانب العديد من الفوائد الصحية المحتملة الأخرى. في الختام ، عززت النتائج التي توصلنا إليها القيمة الطبية والدوائية والثقافية والممارسات العلاجية لـ N. sativa ، والتي ربما تساعد الباحثين في الاقتراب من فائدة وفعالية وفعالية هذه العشبة. ومع ذلك ، فإن دمج هذه النباتات في تطوير وإنشاء أدوية جديدة لعلاج العديد من الأمراض لم يتم استغلاله بالكامل بعد. بموجب هذا ، تقدم هذه المراجعة مسحًا تفصيليًا للأدبيات العلمية المتعلقة بالخصائص الدوائية والمكونات الكيميائية والتأثيرات البيولوجية لبذور هذه العشبة.

## 1. Introduction:

In recent years, literature on the therapy of many ailments using natural products has been increasing lengthily owing to their promising results as well as uncommon negative effects (Al-Attass et al., 2016). Recently is a huge rise in the use of medicinal herbs, compared to chemical medications. This can be attributed to many considerations, such as ease of over-the-counter access, low price, no need to speak to healthcare specialists, in addition to belief in diminishing side effects of natural herbal remedies. Herbal therapies that have been proven to work, which rank greatly as a "wonder seed" is Nigella (Ahmad et al., 2013; Yimer et al., 2019). The significance of *Nigella sativa* to the Islamic culture came from saying "In the black seed is the remedy for each ailment except death," according to the Prophet Mohammed's holy teaching (Ghaznavi, 1991). It is exactly the same sort of black cumin that the Messenger of god Muhammad described as a treatment for all illnesses, but it does not prevent old age or death. *Nigella sativa* is a well-known medicinal plant with a wide range of therapeutic properties, like antidiabetic, anti-microbial, anti-inflammation, anti-tumor influences, besides many other various diseases in Middle East, little Asian countries, Southern Europe to many decades (Gholamnezhad et al., 2016). Medicinal influences of Nigella might be due to its numerous active constituents, like thymoquinone, thymol, and Nigellone (Gholamnezhad et al., 2016; Majdalawieh AF, and Fayyad MW. 2015). However, thymoquinone is the most biologically active ingredient isolated from the seeds of Nigella sativa. In recent centuries, Nigella sativa has become a major research area, and it has a number of traditional applications, so it has already been studied a lot for its bioactive constituents and medicinal uses.

## 2. Plant's morphology:

Nigella sativa is a tiny yearly herb that produces to a tallness of fifty to sixty cm. Its leaves are alienated into 2 to 3 cm long linear segments that grow on both sides of the stem that develop in pairs. It has long upper leaves and short, petiolate below leaves. Flowers on solitary long peduncles are fragile, light, and blue. Nigella sativa reproduces by forming a capsule containing a large number of white trigonal seeds.

When the capsule has developed, it releases up and the seeds inside are opened to the air, turning dark in color. The seeds have a strong pungent flavor and are triangular in shape (Chevallier, 1996).

**Figure 1**: Nigella sativa (B. whole plant, A, D. flowers and C, E. seeds) adopted from internet.

## 3. Scientific Classification

Kingdom: Plantae

Division: Magnoliophyta

Order: Ranunculales

Family: Ranunculaceae

Genus: Nigella

Species: sativa (Kooti et al., 2016)

## 4. Chemical constituents

Nigella sativa seed involves: proteins, saponin, alkaloid, and oil like fatty acids that aren't saturated such as almitoleic, sterol esters, linolenic, sterol glucosides, stearic and myristic acid like linoleic, oleic, beta-sitosterol, palmitic, eicosadienoic, cycloartenol, arachidonic, and cycloeucalenol (Tembhurne et al., 2014; Ahmad et

al., 2013; Staphylakis PK, and Gegiou D. 1986). Oil is a highly volatile commodity (0.4-0.45 %) comprises saturated fatty acids which comprises: Thymoquinone (TQ), thymohydroquinone (THQ), The nigellone which consider the single part of the carbonyl chain of the oil, limonene, dithymoquinone, alpha and beta pinene, thymol, carvacrol, citronellol, and cymene instable oil of the seed that include: longifoline, carvacrol, p-cymene, 4-terpineol and t-anethole (Tembhurne et al., 2014; Ahmad et al., 2013; Enomoto et al., 2001). Nigella sativa seed possess two various types of alkaloids: isoquinoline type that comprises: nigellicimine, nigellicimine n-oxide and pyrazol type that contains: nigellidine and nigellicine (Tembhurne et al., 2014; Ahmad et al., 2013). Carbohydrates, lipids, vitamins, essential salts, also proteins that including eight or nine necessary amino acids, are all nutritious components of N. sativa. Furthermore, N. sativa seeds comprise alpha hederine, saponin, and trace quantities of limonene, citronellol and carvone, as well as a variety of minerals like Ca, Zn, Cu, Fe, P, K and vitamins (Tembhurne et al., 2014; Ahmad et al., 2013).

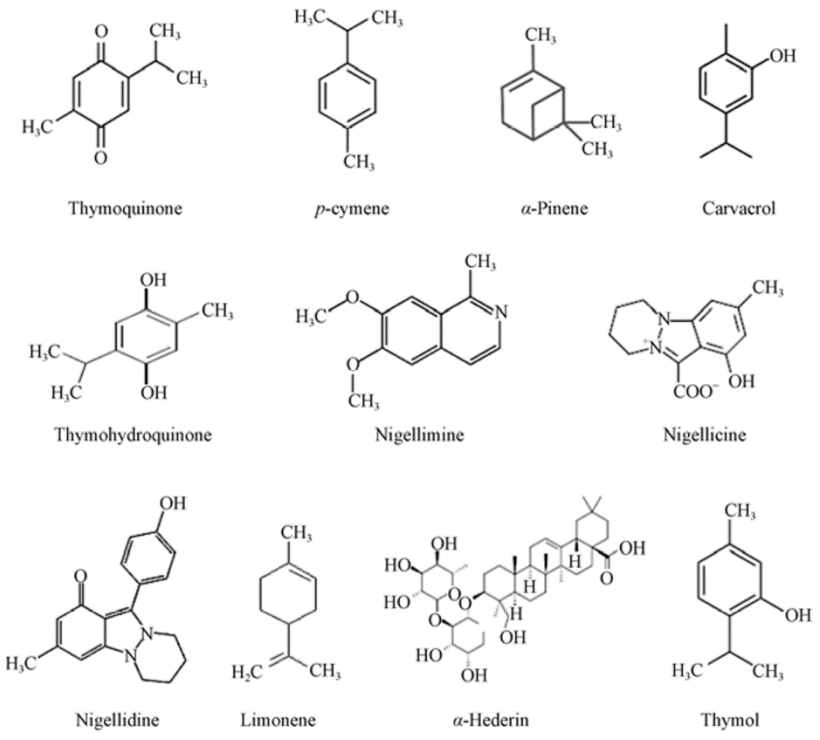


**Figure 2:** Some of the main components of Nigella sativa seeds' chemical structures

(Adopted from Kooti et al., 2016).

**Table 1:** vital component and elements separated from Nigella sativa seeds and their percentages ( Ahmad et al., 2013; Shomar, B. 2012) adopted from (Mohamed et al., 2020).

| Nr. | Compound and elements | Percentages |
|---|---|---|
| 1 | Thymoquinone | 30 up to 48% |
| 2 | Thymohydroquinone, dithymoquinone, *p*-cymene | 7 up to 15% |
| 3 | Carvacrol | 6 up to 12% |
| 4 | 4-Terpineol | 2 up to 7% |
| 5 | *t*-Anethol | 1 up to 4% |
| 6 | Longifolene (a sequiterpene) | 1 up to 8% |
| 7 | nigellicimine n-oxide, nigellicimine, nigellicine, nigellidine, alpha hederine, saponin , limonene, carvone, citronellol | Less than 1% (trace quantities) |
| 8 | Minerals (calcium, manganese, phosphorus, potassium, magnesium, aluminum, copper, zinc, iron,) | Less than 1% (trace quantities) |

**Table 2:** Common components of *Nigella sativa* seeds (adopted from Hamid M. and Hossein H.

2014):

| Component | % Range (w/w) |
|---|---|
| Oil | 31 up to 35.5 |
| Protein | 16 up to 19.9 |
| Carbohydrate | 33 up to 34 |
| Fiber | 4.5 up to 6.5 |
| Saponin | 0.013 |
| Moisture | 5 up to 7 |

**Table 3:** Common components of *Nigella sativa* oils (adopted from Hamid M. and Hossein H.

2014):

| Component | % Range (w/w) |
|---|---|
| Linoleic acid | 44.7 up to 56 |
| Oleic acid | 20.7 up to 24.6 |
| Linolenic acid | 0.6 up to 1.8 |
| Arachidic acid | 2 up to 3 |
| Palmitoleic acid | 3 |
| Eicosadienoic acid | 2 up to 2.5 |
| Palmitic acid | 12 up to 14.3 |
| Stearic acid | 2.7 up to 3 |
| Myristic acid | 0.16 |
| Stroles | 0.5 |

1. **long history of uses in folk remedies:**

Nigella sativa seeds were used in traditional Arabic herbal medication in middle eastern for thousands of years as a spices and food preserving and also for the resistant and therapeutic of various diseases (e.g., headaches, gastrointestinal problems, bronchitis, asthma, skin diseases, influenza, dizziness, conjunctivitis, infections, inflammation, jaundice, anorexia, paralysis, rheumatism, dyspepsia, diabetes, cough, obesity, dysentery, amenorrhea, intrinsic hemorrhage, fever, eczema and hypertension) in Northern Africa, South Asia and Middle East (Bakathir HA and Abbas NA. 2011), (Phillips JD. 1992; Sayed MD. 1982; Burits M and Bucar F. 2000; Rajsekhar S and Kuldeep B. 2011; Merfort et al., 1997; Aboutabl et al., 1986; Warrier et al., 2004; New Delhi. 1989), (Salem, 2005; Ali and Blunden, 2003). A solution extracted from the seeds is beneficial in dropsy, anorexia, dysmenorrhea, indigestion, diarrhea and amenorrhea and use as anti-worms as well as in the therapy of skin rashes. The roasted pills also used to arrest

vomiting (El-Tahir K E and Bakeet DM. 2006; Hosseinzadeh et al., 2007; Ziaee et al., 2012). In this regards, in his famous treatise, Canon of Medicine, Avicenna has mention various Nigella sativa's features, such as energy recovery and weakness enhancement. This herb's health characteristics have also been recognized in Islamic medicine. (Sharma et al., 2009).

2. **Biological activities and pharmacological properties**:

The current article, include some reviewed effects of Nigella sativa on different diseases particularly during the last two decades.

### 6.1. Anti-cancer activity:

Since 428H, Ibn-Sina recognized the anticancer activities of Nigella sativa (Al-Jishi, 2000) and used Nigella sativa for the therapy of tumors, mainly hard spleen tumor. During recent science, perhaps for the first time, the anti-tumor influences of Nigella sativa were observed, when a development of the natural killer cell action, ranging from 200–300%, was showed in advanced cancer patients receiving multi-modality immunotherapy program in which Nigella sativa seed was one of the components (El-Kadi and Kandil, 1986). Recently, several researchers indicate the antineoplastic activities of Nigella sativa seed and its extracts through in vivo using animal models and in vitro using cancer cell lines. According to Salomi et al. (1992), the raw methanolic extract of Black seed had a substantial cytotoxic activity on Elrich ascites carinoma, Dalton's ascites lymphoma, and sarcoma 180, but had no effect on normal lymphocytes. Another study found that the ethyl acetate phase chromatographic component (CC-5) of Nigella sativa ethanolic extract had cytotoxic capabilities against a variety of cancer cell lines, including P388, Hep G2, Molt4, and Lewis lung carcinoma cells (Swamy and Tan, 2000). Furthermore, Nigella sativa seeds given orally protect 80 % of rats from methylnitrosourea-induced oxidative stress and carcinogenesis, and Nigella sativa seeds combined with honey protect 100 % of rats from methylnitrosourea-induced oxidative stress and carcinogenesis. (Mabrouk et al., 2002). Nigella sativa extracts, both aqueous and ethanolic, were found to destroy MCF-7 breast cancer cells (Farah and Begum, 2003). The aqueous extract had a significantly higher

cytotoxic activity than the ethanolic extract, whereas Nigella sativa oil given orally to rats inhibited the induction and improvement of 1,2-dimethylhydrazine-induced abnormal crypt foci, which are putative preneoplastic lesions for colon cancer, without causing any pathological injury to the liver, kidneys, spleen, or other organs (Salim and Fukushima, 2003). The volatile oil of N. sativa is also cytotoxic to human cancer cell lines (SCL, SCl-6, NUGC-4) and the 3T6 fibroblast line (Islam et al., 2004). Worthen et al. (1998) tested the cytotoxicity of a raw gum, a fixed oil, and two purified constituents of the seeds, thymoquinone (TQ) and dithymoquinone (DTM), on numerous parental and multidrug resilient cancer cell lines in vitro. Furthermore, thymoquinone, a cytotoxic molecule separated from Nigella sativa seeds, was previously exclusively found in the ethanolic extract. Consequently, other constituents beyond thymoquinone are likely to have mediated the cytotoxicity of this many herbal preparation's aqueous extract (Samarakoon et al., 2010). In another study, addition to cytotoxic activity of vital oil and extracts of ethyl acetate of Nigella sativa against several tumor cell lines, in vivo animal model (DBA2/P815), the injection of necessary oil into the tumor tissue significantly reduced tumor growth, stopped liver metastasis, and improved the mice's survival chances (Ait Mbarek et al., 2007). Thymoquinone and associated fat soluble compounds have been thoroughly researched and described as having anticancer potential in Nigella sativa extracts with organic solvents. However, as mentioned above in some investigations, the aqueous extract of N. sativa seed presented antitumor influence, suggesting the presence of water soluble active ingredients. This effect was recently confirmed when Nigella sativa aqueous extract significantly increased NK cytotoxic action against YAC-1 cancer cells (Majdalawieh et al., 2010).

### 6.2. Antioxidant activity:

Several previous studies have identified the anti-oxidant capabilities of Nigella sativa seeds. Nigella sativa may be useful in the fight against and treatment of brain ischemia and neurodegenerative illnesses due to its anti-oxidant characteristics (Mahmoud et al., 2002). Free radical production could be at least partially to blame for various human sicknesses and disorders. As a result, Nigella

sativa's antioxidant properties may have contributed to its usage in traditional medication. The antioxidant properties of Nigella sativa crude extract were investigated. The vital extracts, thymoquinone, and other compounds such as anethole, carvacrol, and 4-terpineol all showed promising radical scavenging abilities. The chemiluminescence and spectrophotometer procedures were used to test the free radical scavenging impact of thymoquinone, dithymoquinone, and thymol on reactions producing reactive oxygen species such as superoxide anion radical, hydroxyl radical, and singlet oxygen (Kruk et al., 2000). In addition, thymoquinone inhibits iron-dependent lipid peroxidation in a concentration-dependent manner (Nagi MN and Mansour MA. 2000). As a result, thymoquinone can lower oxidative stress and promote antioxidant defenses in the body. Therapy with thymoquinone results in a decrease in malondialdehyde and other oxidative stress indicators, as well as a rise in total thiol content and glutathione levels (Seronello et al., 2007; Mohamed et al., 2005; El-Tawil O and Moussa SZ. 2006). Protein deactivation, protein oxidation, calcium balance disturbances, lipid peroxidation, and consequent loss of cell viability can all be induced by oxidative stress reduction (El-Tawil O and Moussa SZ. 2006). Moreover, reduction of free radicals with thymoquinone can also reduce the chance of free radicals damaging DNA and causing cancer (Burits M and Bucar F. 2000; Fouda et al., 2014). By boosting the capabilities of quinone reductase and glutathione transferase, oral injection of thymoquinone is a prospective preventive drug against hepatocarcinogenesis and damage in liver tissues (Sayed-Ahmed et al., 2010).

### 6.3. Anti-inflammatory activity:

Many acute and chronic disorders include inflammation as one of their key pathophysiological features (Zahra et al., 2016). Contagion and oxidative stress increase the expression of inflammatory genes, which leads to an increase in inflammatory mediators such as cytokines, eicosanoids, oxidants, and lytic enzymes. As a result, introducing a multipotential and preventive agent in the therapy of inflammatory illnesses is promising (Zahra et al., 2016). Also, thymoquinone and other fixed oil from the seeds were found to treat skin rashes,

rheumatism and back pain (Umar et al., 2012) and a considerable reduction in rat paw edema and granuloma pouch weight, as well as reduced membrane fat peroxidation and eicosanoid production in leucocytes ( Sharma et al., 2009). Moreover, thymoquinone has anti-inflammatory properties in a variety of inflammatory illnesses. (Mansour M and Tornhamre S. 2004; Mahgoub A. 2003; Tekeoglu et al., 2007). Inflammatory cytokines can also activate signaling pathways in hepatocellular that cause cell injury. By reducing the enzymes cyclooxygenase and lipoxygenase, thymoquinone is an efficient reduction of eicosanoid synthesis, specifically thromboxane B2 and leukotriene B4. One of most significant mediators are the development of bleb in hepatocyte cell membranes and the promotion of free radical generation (El-Tawil O and Moussa SZ. 2006). Thymoquinone reduces inflammation by lowering malondialdehyde level, fat peroxidation products and reducing cytokines by suppressing NF-B activity, and decreasing cytochrome c synthesis from mitochondria by preventing the creation of reactive oxygen species (ROS) in the liver (Badary et al., 2000).

### 6.4. Antidiabetic activity:

Several traditional medicine experts recommended by Nigella sativa to treatment diabetes (Ali B and Blunden G. 2003). Previous research has shown that Nigella sativa has therapeutic properties for fat and carbohydrate metabolism disturbances. Nigella sativa has been demonstrated to have a therapeutic influence on metabolic parameters in diabetes in a number of animal and clinical investigations (Heshmati and Namazi. 2015). Nigella sativa has been shown to have significant blood glucose lowering properties, this could be owing to the presence of essential oil (Al Yahya M. 1986). The antidiabetic effects of Nigella sativa are assumed to be caused by the stimulation of (AMPK), which affects cellular absorption from hypolipidemic and antidiabetic proteins. In this context, the evidence and traditional use of Nigella sativa's hypolipidemic and hypoglycemic effects among diabetic's patients and those with metabolic syndrome have been explored in several clinical research (Bamosa, 2010; Sabzghabaee, 2012). Similarly, a clinical trial of Nigella sativa on sixty diabetic individuals revealed significant enhancements in total cholesterol, it is active as an

add-on medication in patients with insulin resistance syndrome, as measured by little density lipoprotein cholesterol (LDL- C) and fasting blood sugar levels. (Najmi et al., 2008). In a study conducted by Nadia and Taha (2009), they analyzed the effects of Nigella sativa essential oils and thymoquinone on oxidative stress and neuropathy in Streptozotocin-caused diabetic animals. The results demonstrated a large rise in norepinephrine and dopamine levels, as well as a significant drop in serotonin content, as compared to the control group. Oral Nigella sativa oil or TQ injections partially reversed these effects (Tembhurne et al., 2011). According to the findings, total antioxidant capacity (TAC), catalase (CAT), glutathione (GSH), and superoxide dismutase (SOD) all increased significantly after Nigella sativa intake, as did the level of thiobarbituric acid-reactive substances (TBARS). There were no important variations in liver and renal function among the two groups, and the blood picture analysis was normal. As a result, continuing Nigella sativa treatment improved blood sugar level and antioxidant equilibrium in type 2 diabetes cases taking oral hypoglycemic medications (Kaatabi et al., 2015). In streptozotocin-diabetic rats, Nigella sativa extract resulted in beta cell regeneration and relative proliferation, as well as a reduction in free radical creation (Benhaddou-Andaloussi et al., 2011; Ramadan et al., 2003). Supplementing rats with Nigella sativa extract and oil, as well as TQ, lowers tissue MDA and blood glucose while increasing serum insulin and tissue SOD level. These results imply that Nigella sativa and TQ may be effective in the therapy of diabetes and the prevention of oxidative stress in β-cells (Kanter et al., 2003). TQ (in drinking water) and Nigella sativa powder (matched with edible food) were administrated to rats over a period of 25 days, and the studied hematology indicators revealed that TQ and Nigella sativa caused a important reduction in blood glucose. (Abdelmeguid et al., 2010). In rabbits, Nigella sativa extract reduces blood glucose and ceruloplasm and recovers biochemical as well as histological markers of damage liver after two months of treatment. Its antioxidant activities are responsible for these beneficial properties. (Yaman I and Balikci E. 2010). Nigella sativa inhibits gluconeogenesis by regulating the activity of liver enzymes include glucose metabolism. It inhibits the gluconeogenesis enzymes glucose 6-phosphatase and fructose 1.6 bisphosphatase. Also it increases levels of

the glucose 6-phosphate enzyme, which is important in the pentose phosphate circus in cells. (Wienkötter et al., 2008; Pari L and Sankaranarayanan C. 2009).

**Table 4:** N. sativa and its components have anti-inflammatory and immunomodulatory properties. (adopted from, Zahra et al., 2016).

| Plant extract & doses | Study case | influences | Ref. |
|---|---|---|---|
| Anti-inflammatory | | | |
| Oil of Nigella sativa (500 mg twice a day) | Patients with rheumatoid arthritis | ↓ disease activity score, swollen joints, and morning stiffness length | (Gheita and Kenawy, 2012) |
| Thymoquinone | Cells of human blood | Both 5-lipoxygenase and LTC4 synthase pathways are inhibited. | (Mansour and Tornhamre, 2004) |
| Immunomodulatory | | | |
| Nigella sativa (1g b.i.d. for 4 weeks) | Volunteers from human | ↑ CD4+/CD8+ Natural killer (NK) cell function and T cell ratio | (El Kadi et al., 1990) |
| Nigella sativa (whole plant) and its refined proteins | Mononuclear cells from human peripheral blood (PBMC) | mixed lymphocyte cultures, stimulatory and suppressive effects | (Haq et al., 1999) |
| Nigella sativa (whole plant) and its refined proteins | PBMCs were activated by the pokeweed mitogen (PWM) | Effects on lymphocytes that are suppressive, ↑IL-8, and TNFα | (Haq et al., 1999) |
| Nigella sativa (whole plant) | PBMCs that have not been activated | ↑IL-1beta secretion and TNFα, ↓IL-8 | (Haq et al., 1999) |
| RPMI seed solution of Nigella sativa | PBMC of Human | Mitogen-stimulated T cells and macrophages are inhibited. | (Winkler et al., 2008) |

| | | | |
|---|---|---|---|
| Nigella sativa oil (40–80 mg/kg/day) | Atopic eczema, bronchial asthma, and allergic rhinitis patients | ↓IgE and eosinophil count, ↓in plasma T and ↑ no change in HDL cholesterol, lymphocyte subpopulations, endogenous cortisol levels, or ACTH release. | (Kalus et al., 2003) |
| Ointments containing Nigella sativa | Patients with eczema on their hands | Hand eczema has improved, ↓ dermatology life quality index I scores. | (Yousefi et al., 2013) |
| 30 days of Nigella sativa oil | Patients suffering from allergic rhinitis | ↓ Nasal mucosal congestion, itching, runny nose, sneezing bouts, turbinate hypertrophy, and mucosal pallor | (Nikakhlagh et al., 2011) |
| 30 days of Nigella sativa seed (2 g/day orally) | Patients suffering from allergic rhinitis | ↑PMN functions, ↑ CD8 counts | (Isik et al., 2010) |
| For 6 months, use Nigella sativa oil twice daily on lesions. | Vitiligo patients have vitiligo lesions on their skin. | ↓ The size of the lesions on the patient's body | (Ghorbanibirgani et al., 2014) |

## 6.5. Antimicrobial activity:

Nigella sativa oil and extracts have been demonstrated in numerous studies to exhibit antimicrobial activity against a wide range of microbes, including those resistant to antibiotics (Kamil ZH. 2013; Toama et al., 1974). Nigella sativa extracts were tested for antimicrobial influence against Staphylococcus aureus, Pseudomonas aeruginosa and E. coli, and Candida albicans, a harmful fungi (Morsi NM. 2000). Nigella sativa's antimicrobial properties are attributed to active components such as melanin and thymohydroquinone (Al Yahya M. 1986). In vitro

antimicrobial influence of Nigella sativa oil on various types of bacteria including eleven gram-negative, three gram-positive, and C. albicans yeast revealed that all species were very sensitive (Hanafy M, Hatem M. 199). Morsi NM. (2000) showed that, after subcutaneous injection, Nigella sativa extract successfully destroyed harmfull staphylococcal contagion in mice. Several studies have found that Nigella sativa extracts work in tandem with gentamicin and other antibiotics, cephalexin, terbinafine, chloramphenicol, nalidixic acid, streptomycin, doxycycline and ampicillin to eradicate E. coli. (Morsi NM. 2000; Ara et al., 2005). Additionally, Yersinia enterocolitica, Pasteurella multocida, Trueperella pyogenes, Corynebacterium pseudotuberculosis, Listeria monocytogenes, Corynebacterium renale, Mannheimia haemolytica, Brucella abortus, E. coli, and S. aureus are among the bacteria that Nigella sativa inhibits. (Namjoo et al., 2013). According to another study, NSO has anti-bacterial activity similar to antibiotics like ceftazidime, cefaclor, cefamandol, and cefuroxime (Gharibi et al., 2012). Likewise, Nigella sativa's antifungal properties for methanolic extraction is demonstrated. In mice, it had an inhibiting effect on candidiasis. (Niakan et al., 2006). In a study, the antidermatophyte effectiveness of Nigella sativa thymoquinone and other extracts were evaluated beside eight fungal infections: 4 Trichophyton rubrum types and one each of Microsporum canis Trichophyton mentagrophytes, Trichophyton interdigitale, and Epidermophyton floccosum (Bita et al., 2012). Garlic extracts and NSO both have oxidative and antischistosomal properties that investigated in several studies. The findings show that GE and NSO protection considerably improves the oxidant resistant properties of schistosomiasis mice compared to non-treated infected mice and prevents the majority of biochemical and blood abnormalities. (Aljabre et al., 2005). Similarly, the actions of NSO in injury hepatocytes produced by the infection of mice with S. mansoni were observed by Mahmoud et al. Infection with S. mansoni causes a important rise in serum ALP, ALT and GGT activity, with a minor rise in ALP quantity, however decreasing the level of albumin. Injection of NSO enhances the alterations in GGT, ALT, and AP action, in addition to the albumin level (Shenawy et al., 2008). Moreover, the antibacterial properties of TQ at low doses suggested the need for more in vivo research. As a result, future research should focus on isolating and

formulating novel antibacterial elements from this herb, as well as conducting more clinical trials.

**Table 5:** Antitumor influences of Nigella sativa and its components (adopted from, Zahra et al., 2016).

| Plant extract & doses | Study case | Influences | Ref. |
|---|---|---|---|
| Nigella sativa seed oil and extract | Lung cancer cell line from a human | ↓ Cancer cell viability and alterations in cellular morphology | (Al-Sheddi et al., 2014) |
| Nigella sativa oil | Monocytes and macrophages from humans | In monocytes and monocyte-derived macrophages, there is a regulatory influence on cell proliferation and differentiation. | (Mat et al., 2011) |
| N. sativa seed extracts' lipid fraction | MCF-7 human breast cancer cells | At low doses, cytotoxic to MCF-7 cells | (Mahmoud and Torchilin, 2013) |
| Nigella sativa seed aqueous extract | MCF-7 human breast cancer cells | Aqueous extract cytotoxicity at high concentrations and hormetic impact at low concentrations | (Mahmoud and Torchilin, 2013) |
| Oil nanoemulsion adjuvant treatment | MCF-7 human breast cancer cells | ↑ Doxorubicin's antitumor action | (Mahmoud and Torchilin, 2013) |
| Nigella sativa hydroalcoholic extract, n-hexane, and ethyl acetate fractions | Human renal adenocarcinoma (ACHN) and normal renal epithelial (GP-293) cell lines | ↓ ACHN cell viability is affected by dose and time. Total extract caused more significant morphological alterations and apoptotic effect in ACHN cells than in GP-293 cells. | (Shahraki et al., 2015) |

| | | | |
|---|---|---|---|
| Thymoquinone | Human colon cancer cells HCT-116 | TQ induces apoptosis in HCT-116 cells (through Bcl-2 protein and p53 mRNA expression). | (Gali-Muhtasib et al., 2004) |
| Thymoquinone | Osteosarcoma cell line from a human (SaOS-2) | Apoptotic impact (↓ inhibition of tumor angiogenesis and growth via inhibiting NF-B) | (Peng et al., 2013) |
| Thymoquinone | Endothelial cell of the human umbilical vein | Apoptotic impact (↓ inhibition of tumor angiogenesis and growth via inhibiting NF-B) | (Peng et al., 2013) |
| Thymoquinone | cell lines of Human osteosaroma | In human osteosarcoma cells, p53-independent apoptosis occurs. | (Roepke et al., 2007) |
| Thymoquinone | Cervical squamous cancer cells of humans | Effect on the cells (elevation of p53 and downregulation of the antiapoptotic Bcl-2 protein) | (Ng et al., 2011) |

### 6.6. Antibacterial activity:

Different previous investigation have showed the antibacterial activities of Nigella sativa and TQ on numerous types of bacterial species (Goyal et al., 2017). In many studies TQ and Nigella sativa constituents have revealed a substantial bactericidal effect in contradiction of Gram-positive bacteria and Gram-negative and prevent bacterial production (Kapil et al., 2018; Goel et al., 2018), promising the usage of TQ as a microbial resistant drug in various illnesses (Maideen, N.M.P. 2020; Ahmad et al., 2020). Nigella sativa was studied for bacterial resistant action beside Staphylococcus aureus, Klebsiella pneumoniae, Proteus species, Staphylococcus epidermidis, Enterococcus faecalis, Streptococcus pneumoniae, Porphyromonas species, Acinetobacter baumannii/calcoaceticus, and Veillonella species. (Kiari et al., 2018). The analysis accomplished via the microdilution process showed great antiseptic influences of the vital oil extract of Nigella sativa beside all the examined types of bacteria and mainly *Porphyromonas* sp. And *Staphylococcus*

*epidermidis*. As a result, the agar well diffusion process did not yield perfect findings, indicating that a variety of factors may influence the antibacterial activity of NS extracts. (Kiari et al., 2018). Nigella sativa and its extracts contain antibacterial characteristics that have been recognized since antiquity, and laboratory tries to explain these properties goes back to the early 19th century. (Dorman HJ and Deans SG. 2000). In this regard, the enhancement of resistant bacteria to a number of regularly used antibiotics encourages more research into novel antimicrobial medication to eliminate illness and overcome the challenges of resistance and adverse effects associated with currently used antimicrobial treatments. (Morsi NM. 2000; Hannan et al., 2008). Although the resistant method of Nigella sativa seeds' antimicrobial influence has yet to be determined, its microbial resistant properties might be related to the vital components, mainly the melanin and TQ (Bakathir HA and Abbas NA. 2011). The influence important processes of organisms must be due to the broad scope of their activity (Monika et al., 2013). Furthermore, an additive antibacterial activity with erythromycin, nalidixic acid, doxycycline, spectinomycin, tobramycin, lincomycin, chloramphenicol, ampicillin, and sulfa-methoxazole trimethoprim. (Hanafy MS and Hatem ME. 1991). Many bacterial isolates, including 6 Gram- positive and 16 Gram- negative types of bacteria, were used to estimate the bacterial resistant properties of raw extraction of N. sativa. These separates, notably Gram-negative bacteria, demonstrated multiple antibiotic resistance. The most active fragments were raw alkaloid and a queous extracts, which remained particularly effective against Gram-negative isolates. (Morsi NM. 2000). Beside all species of L monocytogenes, N. sativa extracts demonstrated powerful antibacterial influences, resulting in a substantially larger inhibition zone than gentamicin (P0.01). N. sativa and gentamicin formed mean inhibition zones of 31.50 ±1.0 and 14.80 ± 0.50 mm, respectively. (Nair et al., 2005). MRSA, or methicillin resistant Staph. aureus, is consider the greatest common diseases found in laboratories and clinics. The ethanolic extract at a dose 4 mg/discs was shown to be sensitive to the majority of MRSA strains tested; the extract had a lowest inhibitory concentration (MIC) range of 0.2-0.5 mg/ml. (Hannan et al., 2008). Antibiotics may enhance TQ's antibacterial activities, particularly with Staph. aureus. TQ and HQ were found to

have antibacterial properties against E. coli, Salmonella typhimurium, Pseudobacterium aeruginosa, Shigella flexneri, Salmonella enteritidis, and Staph. aureus in a study. TQ was found to be particularly effective against Staph. aureus, with concentrations of three and six g/ml being enough to prevent and destroy the organism, respectively. Compared to methanol extract, N. sativa aqueous extracts showed less antibacterial activity.

### 6.7. Antiparasitic activity:

In other studies, the antiparasitic properties of Nigella sativa seeds were investigated. Nigella sativa is thought to be a beneficial ingredient for preventing and treating parasitic illnesses. However, Nigella sativa oil has been shown to have antinematodal and anticestodal activities. Moreover, Nigella sativa oil was found to be beneficial in decreasing the quantity of Schistosoma mansoni worms inside hepatic duct as well as the overall amount of ova placed in hepatic duct and gut. (Mahmoud et al., 2002; El-Shenawy et al., 2008). Other parasitic worms, such as Hymenolepis nana, have lately been found to be resistant to Nigella sativa (Ayaz et al., 2007). It accomplishes this by boosting the host's immunity. Other worms, such as Trichinella spiralis and Aspiculuris, were studied for similar defensive benefits. (AbuElEzz, 2005). The influences of N. sativa seeds were studied in youngsters who were commonly infested with cestode worms. At the levels examined, oral treatment of a dose (40 mg/kg) N. sativa ethanolic extract decreased the ratio of fecal ova (Akhtar MS and Riffat S. 1991). Moreover, the antimalarial activities is attributed to MENS having an antioxidant influence in mice infested with *Plasmodium*, which improves the oxidative state in erythrocytes, and liver cells of infected mice were also seen (Okeola et al., 2011). Rabbits were given 400 mg/kg of aqueous extracts and seeds oil emulsification to treat coccidiosis. Both treatments had anticoccidial effects, although the N. sativa oil emulsion had a faster antiparasite effect. Both treatments improved the histology of the liver tissue and promoted weight increase and a reduction in the detaching of fecal ova. The improvements involved a substantial decrease in inflammatory cell penetration in portal area, as well as a reduction in several phases of worms in the biliary canals, as well as hemorrhage among liver lobules,

hepatic cells returning to their normal circular preparation, as well as totally intense indicators disappearing. Alkaloid nigellicine, which own a fatal effect on worms, is found in higher concentrations in the N. sativa oil emulsion (Baghdadi HB and Al-Mathal EM. 2011). The efficacy of NSO and TQ to decrease the cytogenetic harm induced by schistosomiasis infection also contributes to the protection (Aboul-Ela EI. 2002).

**Table 6:** N. sativa and its constituents have anti-diabetic, anti-hyperlipidemic, hepatoprotective, and other effects on metabolic syndrome. (Adopted from, Zahra et al., 2016).

| Plant extract & doses | Study case | Influences | Ref. |
|---|---|---|---|
| For 12 weeks, take 2mg of Nigella sativa seed every day. | Adjuvant treatment for patients with type 2 diabetes | ↓ Insulin resistance, FBS, 2hPG, HbAlc, and FBS | (Bamosa et al., 2010) |
| 2 grams of Nigella sativa seed each day for a year | Adjuvant treatment for patients with type 2 diabetes | ↓ Insulin resistance, FBG, and HbA1c; ↑β-cell activity; ↑ all antioxidants: TAC, SOD, CAT, and glutathione, ↓TBARS | (Kaatabi et al., 2015) |
| 3 months of Nigella sativa oil (2.5 ml) | Adjuvant treatment for patients with type 2 diabetes | ↓ (BMI), HbA1C, FBS, 2hPG and lipid profile | (Hosseini et al., 2013) |
| 12 weeks of Nigella sativa oil (3g/day) | Adjuvant treatment for patients with type 2 diabetes | ↓ NS changes in TC, HDL-C, insulin secretion; NS changes in weight and BMI FBS, HbA1c, TG, and LDL-C | (Heshmati et al., 2015) |
| Nigella sativa seed + Trigonella foenum-graecum (250 mg) | Adjuvant treatment for patients with type 2 diabetes | ↑ HDL-C; NS triglyceride and creatinine changes | (Memon et al., 2012) |

| | | | |
|---|---|---|---|
| Nigella sativa seed powder (500 mg/day) | Patients suffering from metabolic syndrome | ↓ Blood sugar levels: FBG, PPBG, HbA1c, and LDL-C. | (Najmi et al., 2012) |
| 6 weeks of Nigella sativa oil (2.5 mL twice daily) | Patients suffering from metabolic syndrome | ↓FBG, LDL-C and TC. | (Haque et al., 2011) |
| Treatment with Nigella sativa (2mg/day) | Patients with hyperlipidemia | ↓ NS changes in FBS, HDL-C; TC, and LDL-C | (Sabzghabaee et al., 2012) |
| 2 months of Nigella sativa powder (1g/day) | Patients with high cholesterol levels are called hypercholesterolemics. | ↓TC, TG, HDL-C and LDL-C | (Bhatti et al., 2009) |
| 8 weeks of Nigella sativa powder (2 g/day) | Females that are overweight | ↓TC, TG, LDL-C, and ↑ HDL-C | (Farzaneh et al., 2014) |
| 2 months of Nigella sativa powder (1g/day) | Women who have reached menopause | ↓TC, TG LDL and ↑HDL-C | (Ibrahim et al., 2014b) |
| 12 weeks of Nigella sativa seed (1.6 g/day) | Premenopausal ladies are women who have not yet reached menopause. | ↓ NS changes in TC, TG, and HDL-C; BG and LDL | (Latiff et al., 2014) |
| Allium Sativum oil + Nigella sativa seed (500 mg-250 mg) | Dylipidemia caused by psoriasis | ↓Non-HDL, LDL, TG and cholesterol, and ↑HDL | (Ahmad Alobaidi, 2014) |
| Extract of ethanol (10–100 mg/ml) | Microsomes from human liver (in vitro) | ↓ Metabolites of CYP2D6 and CYP3A4 formation | (Al-Jenoobi et al., 2010) |
| 7 days of ethanolic extract (2.5 g twice daily) | Volunteers who are in good health | ↓ DEX/DOR and DEX/3- MM urinary metabolic ratios | (Al-Jenoobi et al., 2010) |
| *N. sativa* oil (80 mg/kg/day) | ALL children should receive methotrexate treatment. | ↓ Direct, and indirect serum bilirubin; serum ALT, AST, and ALP levels; and prothrombin time | (Hagag et al., 2013) |

HbAlc (glycosylated hemoglobin), CAT (catalase), AST (aspartate transaminase), TAC (total antioxidant capacity), 3-MM (3-methoxymorphinan), SOD (superoxide dismutase), DEX (dextromethorphan), TBARS (thiobarbituric acid reactive substances), NS (Not Significant), DOR (dextrorphan) and ALT (alanine transaminase).

### 6.8. Antiviral effects:

Viral infections produce apoptosis, which results in a loss of lymphocytes in the recipient cell. Antioxidants be able to prevent viral apoptosis as well as inhibit viral repetition in target cells, therefore antiviral and antioxidant actions can be related. (Peterhans E. 1997). Murine cytomegalovirus (MCMV) was employed as a model to assess the antiviral properties of Nigella Sativa oil. On the third day of infestation, mice were given an intraperitoneal injection of Nigella Sativa oil, which revealed viral titers in the liver and spleen. The viral burden in the liver and spleen of control mice was 45×104 vs. 7×104 and 23×103 vs. 31×03, respectively, compared to Nigella Sativa oil treated mice. This antiviral activity was accompanied by a rise in interferon-gamma levels in blood, in addition to a rise in the number of CD4+ helper T cells, suppressor function, and macrophage quantities. On the 10$^{th}$ day following infection, the viral level in the liver and spleen of NSO-treated mice was undetectable, while it was visible in animals treated, indicating that in vivo therapy with N. sativa oil elicited strong antiviral influences against MCMV infection (Salem ML and Hossain MS. 2000). The NSO's antiviral actions are linked to an increase in CD4 cell responsiveness (Salem ML and Hossain MS. 2000).

### 6.9. Antifungal activity:

Different studies showed that, against numerous strains of Candida albicans, methanolic extracts of Nigella sativa show the greatest antifungal activity, followed by chloroform extracts. There was no antifungal activity for aqueous extracts. Candida albicans colonies were developed in the liver, kidneys, and spleen after an intravenous inoculum was given. Administration of mice with N. sativa extract 24 hours after injection had a strong decreasing effect on the organism's development in all organs tested. In 2003, Khan et al. discovered that an aqueous extract of Nigella sativa seeds had a decreasing activity on candida infection in mice. In the

groups that injected with the N. sativa extract, there was a five-fold drop in Candida in the kidneys, an eight-fold decrease in the liver, and an 11-fold decrease in the spleen. Histopathological testing of the various organs supported these findings (Bita et al., 2012). These findings support the use of N. sativa in folk medicine for the therapy of fungal skin infections due to its influence as a source of antidermatophyte medicines (Aljabre et al., 2005). The anti-yeast properties of dithymoquinone, TQ, quinines, and thymohydroquinone from N. sativa seeds were established in vitro in contradiction of six dairy spoilage yeast types using a broth microdilution process. At two pH levels (4.0 and 5.5), the antifungal activities of the quinones were in comparison to the usual preservatives used in milk yields (calcium propionate, potassium sorbate and natamycin), while thymohydroquinone and TQ have significant antiyeast effects. (Halamova et al., 2010). Ns-D1 and Ns-D2, two novel antifungal defensins, were isolated and sequenced from N. sativa seeds. The antifungal actions of the Ns-D1 and Ns-D2 defensins against a variety of phytopathogenic fungi were quite different (Rogozhin et al., 2011). The mechanism is thought to be because to defenses interacting with certain sphingolipids on fungal membranes (Rogozhin et al., 2011).

### 6.10. Antifertility activity:

The antifertility effects of Nigella sativa among male rats were investigated. Sperm production was inhibited, and the sialic acid concentration of prostate, vesicula seminals, epididymis, and the testis, was significantly reduced. (Sharma et al., 2009). Oral injection of Hexane extract of N. sativa seeds L. at a dose of 2 g/kg daily on days 1 -10 postcoitum stopped pregnancy in rats. While Hexane extract of N. sativa seeds showed substantial anti-fertility effects in column fractions and sub-fractions. The active hexane extract had only a moderate uterotrophic effect at contraceptive doses, similar to 0.002 mg/kg doses of 17 varies; is directly related to-ethinylestradiol, nonetheless had no estrogenicity in the young rat bioassay (Keshri et al., 1995). In male rats, an alcoholic extract of Nigella sativa seeds was reported to have anti-fertility influences, possibly due to Nigella sativa's innate estrogenic properties. (Agarwal et al., 1990).

### 6.11. Antimalarial activity:

Several Nigella sativa extracts have been found to have antiplasmodial properties in each in vivo and in vitro plasmodia pathogens. At a dosage of 50 ug/ml, it completely inhibits parasite growth (Plasmodium falciparum). Nigella sativa has antiparasitic action that is dose dependent (Abdulelah et al., 2007; El-Hadi et al., 2010).

### 6.12. Anti-ulcer activity:

Nigella sativa seeds, aqueous extract was found to be efficient in lowering the ulcer rate produced by aspirin by 36% (Rajkapoor et al., 1996). In another investigation, NSO was discovered to own a protective influence against the development of stress gastritis in hypothyroidal rats (Khaled et al., 2009). The elimination of Helicobacter pylori in individuals with non-ulcer dyspepsia also supports the recent clinical investigation (Salem et al., 2010).

### Cardiovascular-protective activity:

Nigella sativa has been shown to protect against diabetes, platelet aggregation, blood pressure disorder, heart rate lipid levels alteration, endothelial malfunction, metabolic syndrome, atherogenesis, heart mass and muscle contraction irregularity and cardiotoxicity in numerous in vitro and in vivo experimental animal studies. As a result, N. sativa able to employed as a defensive and helpful mediator in cardiovascular illnesses as a harmless multi-properties herb with effective antioxidant and anti-inflammatory effects (Shabana et al., 2013). A little studies have looked at the cardio-protective properties of Nigella sativa and its components in both animal and human studies, with mixed results. Dehkordi et al. (2008) discovered that a two-month oral injection of N. sativa seed extract had a decreasing blood pressure influence in individuals with moderate hypertensive. When compared to the baseline, systolic pressure (SBP) and diastolic pressure (DBP) were considerably lower after administration with 2.7 and 5.3 mg/kg/day of the herb extracts. Furthermore, when compared to baseline data, N. sativa administration considerably lowered complete and LDL-C amounts (Zahra et al.,

2016). The preventive effect of N. sativa on the thorax aorta contractile response is examined in a model in rats of diabetes mellitus. The results reveal that treating diabetic rats with this plant reduces the contractile response to non-specific KCL agonist and specific adrenergic receptors agonist to the greatest extent possible. Long-term oral N. sativa injections may lower arterial contractile reactivity and the amount of heart problems in diabetics (Fararh et al., 2004). Previous research has revealed that the actions of N. sativa have been documented on cardiac effects in diabetic rabbits, with the findings showing that N. sativa extract moderates unbalanced heart influence in diabetic rats (Roughani et al., 2006). TQ's protective activities and the severe (at 4 and 18 h) impact of diesel exhaust particles (DEP) on cardiovascular and pulmonary factors in mice were also studied, with the findings revealing that TQ therapy lowers systolic pressure, inhibits leukocytosis and IL-6 production, and reduces plasma SOD effects. As well as prevents the numbers of platelets from dwindling and prothrombotic proceedings from occurring (Meral et al., 2004). In addition, the influence of NSO on cholesterol, blood glucose levels, and homeostatic balance in rats have been investigated, with the results indicating a decrease in cholesterol, glucose, TG and an increase in white blood cells, hematocrit, platelets, and hemoglobin. Nigella sativa extract injection at 800 mg kg-1 for 3 months reduced heart tissue injury induced by ischemia reperfusion, which was likely related to Nigella sativa's anti-oxidant activity (Nemmar et al., 2011). In anesthetized rats, injection of a required oil ingredient at 4–32 μg·mL–1 resulted in a dose-dependent decreasing in blood pressure and heart contraction, which was reduced by anticholinergics (Amarouch et al., 2002). Another study indicated that dichloromethane N. sativa extract (0.6 mL·kg–1·d–1) lowers mean blood pressure in spontaneously hypertensive rats (El Tahir et al., 1993). N. sativa is used to treat hypertension alone or in conjunction with honey or garlic, which prompted El-Tahir et al. (1993) to examine the effects of the instable oil of N. sativa and its essential ingredient thymoquinone on the blood pressure and heart contraction of anaesthetized rats. The heart contraction and blood pressure are reduced by both drugs by the dose-dependent method. Cyproheptadiene, atropine, and hexamethonium greatly inhibited these actions. This indicated that these actions were mostly inhibited centrally via 5-hydroxy

tryptaminergic and muscarinic mechanisms. In spontaneously hypertensive rats, an oral injection dose of 0.6 ml/kg/day of N. sativa extract showed considerable hypotension effects. These findings were equivalent to those of the conventional anti-hypertension medication nifedipine (Zaoui et al., 2002). The drug's influence was attributed in part to its diuretic action, which was associated to 0.5 mg/kg/day furosemide.

**Gastro-protective activity:**

In rats with induced stomach ulcers and gastric basal secretion, the aqueous extract of Nigella sativa exhibits anti-ulcer activities, according to numerous studies. The aqueous extract of Nigella sativa reduced the formation of induced stomach ulcers, according to the findings. In pylorus-ligated Shay rats, this compound also decreased the severity of the ulcer and the amount of acid produced by the stomach during rest. The anti-ulcer influences of Nigella sativa extract are most likely attributable to prostaglandin interactions as well as antioxidant and anti-secretory properties (Zaoui et al., 2000). Furthermore, in rats with aspirin-induced stomach ulcers, Nigella sativa aqueous extract reduces indices by up to 36% (Al Mofleh et al., 2008). Two weeks of supplementation with Nigella sativa extraction at a dose of 0/88 g·kg−1·d−1 raises glutathione and mucin amount in the gut while lowering histamine levels. Hydroalcoholic extract has been researched for its protective effects on the stomach mucosa. (Akhtar et al., 1996). Furthermore, doses of 50 and 100 mg·kg−1 of TQ and Nigella sativa revealed to have a defensive effect on stomach ulcer in rats, reducing ischemia-reperfusion injury and gastric ulcer through their anti-oxidant effects (El-Dakhakhny et al., 2000). TQ therapy can also help to avoided and enhance ulcer, which can be used to treat patients with inflammatory bowel disease (IBD) (El-Abhar et al., 2003). In addition, Mohtashemi et al. show that injecting a honey-based NS oil composition (5 mL NS oil each day) for 8 weeks, compared to placebo, improved indications like dyspepsia intensity and reduced the risk of H. pylori contagion in patients with useful dyspepsia (Mohtashami et al., 2015).

**Hepato-protective activity:**

The influences of ischemia reperfusion damage (CRI) on the liver have been shown to be reduced when given Nigella sativa (0.2 ml/kg) intraperitoneally. Biochemical markers like as aspartate aminotransferase, lactate dehydrogenase, CAT, alanine aminotransferase, oxidative stress index (OSI), TOS, total antioxidant capacity (TAC), and MPO were investigated in hepatic tissues of rats having liver ischemia. According to the findings, Nigella sativa medication keeps the liver of rat from ischemia reperfusion damage (Yildiz et al., 2008). Nigella sativa prevents liver tissues from toxic elements such as lead, as well as reducing hepatic lipid oxidation after exposure to poisons like carbon tetrachloride (Kapoor S. 2009). Cadmium (Cd++) disturbs tissue homeostasis and produces free radicals. The defensive effects of TQ on C d++ liver injury were investigated, with a focus on enzymatic and non-enzymatic antioxidant damage prevention. Under in vitro settings, the protective effects of TQ pretreatment were assessed in post-nuclear supernatant produced from the liver of mice. The antioxidant enzymatic effects were significantly increased after injection with CdCl2 (5 mmol/L). It also resulted in an important rise ($P < 0.001$) in protein carbonyl and a decrease in glutathione concentration. TQ (10 mol/L) pretreatment provided considerable prevention, as shown by decreased protein oxidation and regenerated of cellular fraction-depleted antioxidants. These results support the theory that TQ has a modifying effect on the antioxidant defense system when it is exposed to a toxic shock (Zafeer et al., 2012). Hepatotoxicity is linked to changes in the concentration and effects of enzymes including glutamic-pyruvic transaminase (SGPT), glutamic-oxaloacetic transaminase (SGOT) and the system of oxidative scavenger enzymes like glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD). Using isolated rat hepatocytes, the protective efficacy of thymoquinone against hepatotoxin: terbutyl hydroperoxide was investigated (Daba and Abdel-Rahman, 1998). The hepatoprotective effects of thymoquinone (TQ) were compared to those of silybin, a well-known hepatoprotective drug, in this study. TQ's hepatoprotective mechanism is unknown, although it is likely connected to the protection of intracellular glutathione (GSH), which is recognized to enhance the

vulnerability of cells to irreparable harm when depleted by oxidative stress. It was also discovered that pre-treating rats with Nigella sativa oil for four weeks protected them from CCl4 and D-galactosamine-induced liver damage. When green oil was administered orally with a dose of 100 mg/kg/day for four weeks, no harmful impact on liver function were seen. Thymoquinone with a dose of 8 mg/kg/day for 5 days before and 1 day after CCl4 therapy protected mice from liver histological and biochemical markers impairment (Nagi et al., 1999). It has recently been discovered to have protective properties against ischemia reperfusion damage to the liver (Fahrettin et al., 2008).

**Nephroprotective activity:**

In rabbits, the nephroprotective influences of Nigella sativa oil and vitamin C against gentamicin (GM)-caused nephrotoxicity were studied. For all rabbit groups, blood urea nitrogen, creatinine, and antioxidant effects were examined as indications of kidney injury. When compared to the GM control group, Nigella sativa oil and vitamin C have been demonstrated to have a protective impact on the kidneys by lowering antioxidant influences, blood urea nitrogen and serum creatinine. These two forms of antioxidants have been shown to have synergistic nephroprotective effects when given simultaneously (Saleem et al., 2012). In albino rats, the defensive effects of Nigella sativa oil on kidney toxicity caused by methotrexate were investigated, and this study confirmed the prevention activities of Nigella sativa oil on kidney injury caused by methotrexate (Abul-Nasr et al., 2001). It has been shown that Nigella sativa can protect kidney tissues from ischemia-perfusion injury. MPO, TAC, CAT, OSI, and TOS levels in blood and tissues of kidney were examined. The amounts of blood urea and blood creatinine were also measured. The histology of kidney tissues was also examined. Nigella sativa was found to be beneficial in lowering the amounts of blood urea and creatinine and lowering tubular necrosis scores. Therapy with Nigella sativa lowered TOS and OSI levels while increasing TAC levels in renal tissue and blood. The findings revealed that Nigella sativa had a prevention activity in the rat kidneys against renal I/R damage (Yildiz et al., 2010). The preventive properties of Nigella sativa oil were tested in rats to see if they might prevent cyclosporine A (CsA)-

induced nephrotoxicity. Nigella sativa oil enhanced functional and histological indicators while reducing oxidative stress caused by CsA. Nigella sativa oil defends kidney tissues from oxygen free radicals, which reduces renal damage and morphological irregularities caused by continuous CsA injection (Uz et al., 2008). Nigella sativa in combination with intraperitoneal GM When compared to the GM group, there was a substantial decrease in urea, MDA, NO, creatinine and an increase in SOD and GSH-Px effects, indicating a nephro-protective impact. Nigella sativa inhibits the harmful effects of GM on biochemical and histopathological parameters by acting as a potent free radical scavenger (Yaman I and Balikci E. 2010). Nigella sativa seeds have no effect on biochemical measures of cisplatin-induced nephrotoxicity, despite the fact that the kidneys' histopathologic features have improved after Nigella sativa use (Hadjzadeh et al., 2012). Pretreatment with Nigella sativa oil (5.0 mL·kg−1) reduced plasma transaminase activity, MDA, and TG levels, and improved liver histological alterations in another investigation (Slim et al, 2012).

**Testicular-protective activity:**

Among male C57BL/6 mice, the preventive influence of thymoquinone (TQ) on damage testes caused by methotrexate were investigated. TQ therapy reduced TAC and prevented myeloperoxidase effect from increasing. Mice given methotrexate had interstitial space dilation, a reduction in the diameter of the seminiferous tubules, severe disruption of the seminiferous epithelium, and edema according to light microscopy. TQ may minimize the harmful influences of methotrexate on testes tissues in individuals taking this medication, according to several studies (Gokce et al., 2011).

**Wound healing activity:**

Black seed and oil have been shown to help farm animals recover wounds (Ghonime et al., 2011). In addition, applying a topical therapy ether extract of Nigella sativa seed to staphylococcus-diseased skin in mice promotes therapeutic by lowering total and difference WBC numbers, local contagion and inflammation,

tissue damage and bacterial proliferation (Ahmed et al., 1995). When the activities of cream of silver sulfadiazine (SSD) and Nigella sativa on burn wound therapeutic in an animal model were evaluated, it was discovered that recovering from burns was enhanced in the Nigella sativa and SSD groups in comparison to the control group on the 4, 9, and 14 days (Durmus and Ceribasi, 2010). However, among the 4th, 9th, and 14th days, however, wound curative differed considerably between groups. (Abu-Al-Basal MA. 2011). Despite its non-substantial effects on collagen production, Nigella sativa extracts show greater proliferation of human gingival fibroblasts and faster treatment when comparing to Piper Sarmentosum extracts, Pluchea indica, and Melastoma malabathricum. In addition to boosting bFGF levels until 15% at 100 μg·mL−1 of Nigella sativa, a somewhat healthier activity on TGF-expression was seen. Therefore, N. sativa exhibits hopeful healing effects on wounds, demonstrating its historic usage in the treatment of oral wounds (Osama Abu Zinada, 2009).

**Effect on respiratory system:**

The antispasmodic effects of Nigellone and TQ on the trachea, as well as their activity on the respiratory system, have been studied (Wienkotter et al., 2008). The micro dialysis technique was used to investigate the effects of B a ++ carbachol and leukotriene on tracheal contractions and the transfer of the fluorescent dye rhodamine B in relation to activity of the cilia in the trachea. When the trachea was contracted by the depolarizing impact of Ba2+, Nigellone and great doses of TQ had an inhibitory action that is concentration dependent. The tracheal contractions generated by leukotriene-d (4) LT4 were reduced by nigellone and TQ. In addition, nigellone possesses antispasmodic properties and increases mucociliary clearance, whereas TQ does not. As a result, nigellone not TQ, may be effective in the therapy of certain respiratory disorders (Wienkotter et al., 2008). Relaxant influences of four total concentrations of methanol, n-hexane, aqueous fractions and dichloromethane of Nigella sativa (0.8, 2.0, 1.6 and 1.2 g%) compared to saline solution as a negative control and four total concentrations of theophylline (0.2, 0.4, 0.6 and 0 .8 mmol/L) their sedative properties was tested on guinea pig tracheal chains that had been pre-contracted with 60 mmol/L

potassium chloride (group 1) and 10 μM methacholine (group 2). The findings revealed that most fractions of Nigella sativa have relaxant properties on the guinea pigs' bronchial chains, with the dichloromethane fractions and methanol being more effective (Boskabady et al., 2008). The preventive effect of Nigella sativa on tracheal response (TR) and pulmonary disease in guinea pigs subjected to sulfur mustard was investigated. With n = 6, guinea pigs were administered a dilute solution (ethanol, control group), 100 mg/m3 sulfur mustard breathing (SME group), and SME administered with Nigella sativa, 0.08 g a day (SME + N). TR to methacholine, total lung lavage WBC count, and differential WBC were performed 14 days following exposure. The results propose that Nigella sativa has a protective influence on the TR of guinea pigs exposed to sulfur mustard gas (Hossein et al., 2008). Furthermore, Nigella sativa medication may be effective in the treatment of lung injuries and has therapeutic potential (Kanter M. 2009). The protective effect of NSO was assessed in rats with hyperoxia-induced pulmonary damage, which is expected to promote bronchopulmonary dysplasia in preterm newborns. Chakravarty et al. (1993) demonstrated that nigellone, a thymoquinone carbon polymer derived from Nigella sativa seeds, effectively reduced histamine produce from mast cells in an in vitro investigation, demonstrating the rationale for its traditional usage in asthma. Another study found that giving 15 ml/kg of 0.1 % NS decoction extract for three months resulted in better improvements in PFT parameters and a reduction in asthma symptoms than giving a placebo. (Boskabady et al, 2007). Ahmed et al. studied LRTI patients with wheeze aged 5 to 15 years and found that conventional therapy alone versus conventional treatment with Nigella sativa oil had favorable effects (Ahmad et al., 2009). As a result, conventional treatment with NS oil (0.1 mg/kg) intended for 14 days was found to have greater favorable effects in lowering pulmonic index and rising peak respiration flow rate (Ahmad et al., 2009). Another study found that, daily injections of 0.375 mL/kg of a heated water extract of 50% NS, for two months, when compared to a placebo, there were significant enhancements in PFT and respiratory symptoms for chemical warfare victims. NS was found to have a protective impact on chemical warfare victims, indicating that it was used to protect them (Boskabady MH and Farhadi J. 2008).

**Effect on nervous system:**

The central nervous system (CNS) has been demonstrated to be protected by Nigella sativa seeds, and the most promising narcotic effect perhaps mediated by opioid receptors (Khanna et al., 1993). Neuronal degeneration is reduced by TQ produced from Nigella sativa extract (Houcher et al., 2007). The central nervous system (CNS) is analgesic when using Nigella sativa seed oil. Seizures that are uncontrollable are treated in children with a water extract of Nigella sativa seed (40 mg/kg/8 h) against placebo as therapeutic antiepileptic medication treatment considerably reduced the mean seizure frequency, according to Akhondian et al (Akhondian et al, 2007). While TQ (1 mg/kg) was injected as an adjuvant medication in place of a water extract of Nigella sativa seed in alike medical trial carried out by the same author, the outcomes were comparable (Akhondian et al., 2011). In the LPS-induced depression type, Nigella sativa (200-400 mg·kg−1) caused a reduction in depression in both the forced swim test and the open field test. (Hosseini et al., 2012). NSO has been shown to protect mice from tramadol tolerance and dependence, according to Abdel-Zahir et al. NSO has therapeutic potential by reducing nitric oxide overproduction and oxidative stress caused by drugs (Parvardeh et al., 2005). It has also been shown to enhance the effects of pentobarbitone-induced sleep. The influence of neurotransmitter release on cultured cortical neurons indicated that they imply enhanced neurotransmitter secretion. In cultured neurons, it also controls the release of amino acids. There was an increase in GABA effect, however there was a reduction in glutamate, aspartate and glycine excretion. N. sativa seed extract has relaxing and depression properties which represented in all of the results (Tariq et al., 2010). Intake of Nigella sativa on a regular basis was also shown to lower 5HT turnover and have an anxiolytic influences (Perveen et al., 2009). The major component of nigella seeds is thymoquinone. Thymoquinone was found to have an anticonvulsant action in mice in one investigation (Hosseinzadeh et al., 2004; Hosseinzadeh et al., 2005).

**Effect on the immune system:**

Individuals gain Nigella sativa seeds or oil as a natural medicine to improve their health and avoid colds and Asthama. Several studies have linked Nigella sativa and TQ to immune system activation (Garah et al., 2012; Abdelzaher et al., 2011; Haq et al., 1995). El-Kadi et al. (1986) demonstrated that the effects of Nigella sativa on the immune response, finding that the herb had immuno-potentiating activities in human T-cells in vitro. This was corroborated by Haq et al. (1995), who discovered that Nigella sativa seeds cause T cells to release interleukin-3 and IL-1B. Other research has found that α-linolenic acid, steridonic acid, and other chemicals found in the herb seed improve immune system, notably in T cells (Swamy S and Tan B. 2000; Yehuda S and Carasso RL.1993). Nigella sativa raises the activity of natural killer cells while suppressing T helper cells (Abdel-Zaher et al., 2011). Nigella sativa also has an anti-inflammation and pro-inflammatory cytokine discharge regulating effect. Nigella sativa also affects Th1/Th2 balance and decreases Th2 levels (Işık et al., 2010). The influences of Nigella sativa on immuno-hematological indicators in rainbow trout were investigated in another study, and the results revealed a considerable rising in serum immunoglobulin contents in the therapeutic group (Gholamnezhad et al., 2014). In addition, the immunomodulating properties of a range of medicinal plants, including N. sativa, were tested in BALB/c mice. The findings revealed that N. sativa has an immunoreactive impact and may have treated effects in the protection of opportunistic contagions as well as supportive therapy in neoplastic diseases (Dorucu et al., 2009).

**Reproductive system effect:**

The reproductive organs' weight, as well as the motility and amount of sperm in the caudal epididymis and testicular ducts, are all increased by Nigella sativa seeds. The amount of primary and secondary spermatocytes increases during spermatogenesis. Furthermore, the number of pregnant female rats is increasing (Makhled et al., 2009; Al-Saidi et al., 2009). Infertile men have also been studied for other positive activities of Nigella sativa on Leydig cells, reproductive systems,

and sex hormones (Awad E and Binder B. 2005). Furthermore, when Nigella sativa oil is compared to nicotine on sperm and testes parameters in rats, nicotine reduces the motility and morphology of normal and living sperm, as well as affecting testes tissues, but Nigella sativa oil raises sperm quality and exhibits better testes characteristics of histology (Al- Sa'aidi et al., 2009). In male rats, when comparing the lower and upper dose groups to the control group, the impacts of N. sativa extract on fertility possibility, pituitary-testicular axis hormones, and testosterone showed an important difference in testes and epididymis weight, ESR, sperm count, LH, serum testosterone concentration, DSP and fertility indicator (Ng et al., 2014).

**Table 7:** The anti-infertility characteristics of Nigella sativa and its components, as well as their effects on neurological, cardiovascular, and respiratory diseases (adopted from, Zahra et al., 2016).

| Plant extract & doses | Study case | Effects | References |
|---|---|---|---|
| Effects on the nervous system | | | |
| Seeds of N. sativa (500 mg twice a day for 9 weeks) | Volunteers who are over the age of 65 are needed. | All neuropsychological tests have improved. | (Bin Sayeed et al., 2014) |
| 4 weeks of N. sativa oil | Children with uncontrollable epilepsy | Seizure frequency, intensity, or oxidative stress markers did not vary significantly (TAC and MDA) | (Shawki et al., 2013) |
| (1 mg/kg) thymoquinone | Children with uncontrollable epilepsy | Anti-epileptic properties | (Akhondian et al., 2011) |
| Effects on the cardiovascular system | | | |
| 2 months of N. sativa seed extract | Patient suffers from mild hypertension. | ↓ DBP and SBP; ↓ LDL and TC | (Dehkordi and Kamkhah, 2008) |

| | | | |
|---|---|---|---|
| (100/200 mg twice a day) | | | |
| Seeds of Nigella sativa | Patients over the age of eighteen | There was no discernible reduction in serum lipids, blood sugar, blood pressure, or body weight. | (Qidwai et al., 2009) |
| 8 weeks of N. sativa oil (2.5 ml twice a day) | Volunteers who are in good health | ↓ DBP and SBP | (Fallah Huseini et al., 2013) |
| Effects on the lungs | | | |
| Immunotherapy using N. sativa powder | Mild asthmatic children | There is no influence on the number of Th17 cells. Clinical symptoms have improved. | (Kardani et al., 2013) |
| Immunotherapy using N. sativa powder | Mild asthmatic children | CD4+CD25+ foxp3+Treg and CD4+ IL-10+Treg had no effect. Clinical symptoms are becoming better. | (Susanti et al., 2013) |
| aqueous extract that has been boiled | Patients with asthma | All asthmatic symptoms, asthma symptom/week, chest wheeze, and PFT levels have improved. Inhaler and oral -agonists, oral corticosteroid, oral theophylline, and inhaler corticosteroid usage are all being reduced. | (Boskabady et al., 2007) |
| aqueous extract that has been boiled | Victims of chemical warfare | Inhaler and oral β-agonists, as well as oral corticosteroids, were used less frequently in the study group. | (Boskabady and Farhadi, 2008) |
| aqueous extract that has been boiled | Patients with asthma | Less effective than theophylline in terms of FEV1, PEF, MMEF, MEF75, MEF50, MEF25, and sGaw. | (Boskabady Et al., 2010) |
| Oil of N. sativa | Patients with asthma | PEFR improvement PI decrease | (Ahmad et al., 2010) |
| Infertility-preventative characteristics | | | |

| | | | |
|---|---|---|---|
| 2 months of N. sativa oil (5 ml/12 h) | Men who are unable to conceive | Improves sperm count, motility, morphology, and volume of sperm, as well as pH and roundness of cells. | (Kolahdooz Et al., 2014) |

**Effect on Blood:**

When comparing total time of blood clotting, plasma clotting, and kaolin-cephalin clotting in male rabbits, petroleum ether extract from Nigella sativa was found to reduce total time of blood clotting, plasma clotting, and kaolin-cephalin clotting. Additionally, rats showed a considerable reduction in bleeding time. Although there were no notable changes on prothrombin or thrombin time, the partial time of thromboplastin was reduced while the time of euglobulin was extended (Ghoneim et al., 1982).

**Infertility effect:**

The traditional treatment of Nigella sativa for infertility was established. About 68 infertile males with defective sperm activity were selected based on presence criteria such as aberrant sperm morphology (< 30%), the count of sperm under 20×106/ml, or category A and B motility < 25% and 50%, respectively. Persons were randomly allocated to one of two groups: Nigella sativa oil (n = 34) or placebo (n = 34) and were given the medicine twice a day for two months. At the start and completion of the trial, the major outcomes were sperm count, semen volume, pH, morphology and motility and round cells. The results revealed that ingesting 5 ml of Nigella sativa oil (60 mg/kg/day) for two months enhanced the a count of sperm, appearance, locomotion, pH, the volume of semen, and round cells much more than the control group, with no negative activities. This study determined and presented the fatty acid constituents of the fixed oil and the chemical structure of the volatile oil constituents of the herbal oil. TQ, unsaturated fatty acid, vitamin E, and selenium levels in Nigella sativa oil perhaps accountable for the herb's antioxidant properties (Kolahdooz et al., 2014).

## Conclusion:

Nigella sativa seeds and their extracts are utilized as a natural cure for a variety of ailments all over the world. The constituents of Nigella sativa particularly TQ, have a wide range of health benefits. Studies show that the plant has anti-inflammatory, antidiabetic, anticancer, antimicrobial, antiparasitic, antibacterial, antioxidant, and hepato-renal protective properties, as well as antidiabetic, anticancer, antimicrobial, antiparasitic, antibacterial, and antioxidant properties. Moreover, different studies have looked into its impact on the digestive system, immune system, and nervous system. Further research on the plant's composition and therapeutic capabilities, as well as other unknown traits, is needed before it may be employed as a plant-derived medicine to treat a variety of ailments.

## References:

[1] **Aboutabl EA, El-Azzouny AA, Hammerschmidt FJ. Berlin, New York: Walter de Gruyter and Co; 1986.** Aroma volatiles of Nigella sativa L. seeds. Progress in Essential Oil Research; pp. 49–55. [Google Scholar].

[2] **Abdelmeguid NE, Fakhoury R, Kamal SM, et al.** Effects of Nigella sativa and thymoquinone on biochemical and subcellular changes in pancreatic β-cells of streptozotocin- induced diabetic rats [J]. J Diabetes, 2010, 2(4): 256-266.

[3] **Aboul-Ela EI.** Cytogenetic studies on Nigella sativa seeds extract and thymoquinone on mouse cells infected with schistosomiasis using karyotyping. Mutat Res. 2002; 516:11–17. [PubMed] [Google Scholar]

[4] **Abdulelah HAA, Zainal-Abidin BAH (2007).** In vivo anti-malarial tests of Nigella sativa (Black Seed) different extracts. Am. J. Pharmacol. Toxicol. 2:46-50.

[5] **Abdel-Zaher AO, Abdel-Rahman MS, ELwasei FM.** Protective effect of Nigella sativa oil against tramadol-induced tolerance and dependence in mice: role of nitric oxide and oxidative stress [J]. Neurotoxicology, 2011, 32(6): 725-733.

[6] **Abul-N asr SM, E l-Shafey MDM, Osfor MMH.** Amelioration by Nigella sativa of methotrexate induced toxicity in male albino rats: a biochemical, haematological and histological study. Scintia Agri Bohemica 2001; 32: 123-160.

[7] **Abu-Al-Basal MA.** Influence of Nigella sativa fixed oil on some blood parameters and histopathology of skin in staphylococcal-infected BALB/c mice [J]. Pak J Biol Sci, 2011, 14(23): 1038-1046.

[8] **AbuElEzz NM (2005).** Effect of Nigella sativa and Allium cepa oils on Trichinella spiralis in experimentally infected rats. J. Egypt. Soc. Parasit. 35:511-523.

[9] **Agarwal C, Narula A, Vyas DK, J acob D.** Effect of seeds of kalaunji on fertility and sialic acid content of the reproductive organs of male rat. Geo Bios 1990; 17: 269-272.

[10] **Ahmad, A.; Husain, A.; Mujeeb, M.; Khan, S.A.; Najmi, A.K.; Siddique, N.A.; Damanhouri, Z.A.; Anwar, F.** A review on therapeutic potential of Nigella sativa: A miracle herb. Asian Pac. J. Trop. Biomed. 2013, 3, 337–352.

[11] **Ahmad A, Husain A, Mujeeb M, Khan SA, Najmi AK, Siddique NA, et al.** A review on therapeutic potential of Nigella sativa: A miracle herb. Asian Pac J Trop Biomed. 2013; 3:337–352. [PMC free article] [PubMed] [Google Scholar]

[12] **Ahmed IH, Awad MA, El-Mahdy M, et al.** The effect of some medicinal plant extracts on wound healing in farm animals [J]. Assiut Vet Med J, 1995, 32(64): 236-244.

[13] **Ahmad, M.F.; Ahmad, F.A.; Ashraf, S.A.; Saad, H.H.; Wahab, S.; Khan, M.I.; Ali, M.; Mohan, S.; Hakeem, K.R.; Athar, M.T.; et al.** An updated knowledge of Black seed (Nigella sativa Linn):

Review of phytochemical constituents and pharmacological properties. J. Herb. Med. 2020, 100404. [CrossRef]

[14] **Ahmad, J., Khan, R.A., Malik, M.A., 2010.** A study of Nigella sativa oil in the management of wheeze associated lower respiratory tract illness in children. African Journal of Pharmacy and Pharmacology 4, 436-439.

[15] **Ahmad J, Khan RA, Malik MA.** A study of Nigella sativa oil in the management of wheeze associated lower res- piratory tract illness in children. Afr J Pharm Pharmacol. 2009; 3(5):248-51.

[16] **Ahmad Alobaidi, A.H., 2014.** Effect of Nigella sativa and Allium sativum coadminstered with simvastatin in dyslipidemia patients: a prospective, randomized, double-blind trial. Antiinflamm. Antiallergy Agents Med. Chem. 13, 68-74.

[17] **Akhondian J, Parsa A, Rakhshande H.** The effect of Nigella sativa L. (black cumin seed) on intractable pediatric seizures. Med Sci Monit. 2007; 13(12):CR555-9.

[18] **Akhondian J, Kianifar H, Raoofziaee M, Moayedpour A, Toosi MB, Khajedaluee M.** The effect of thymoquinone on intractable pediatric seizures (pilot study). Epilepsy Res. 2011; 93(1):39-43.

[19] **Akhtar A, Ahmad K, Gilani S, et al.** Antiulcer effects of aqueous extracts of Nigella sativa and Pongamia pinnata in rats [J]. Fitoterapia, 1996, 67: 195-199.

[20] **Akhtar MS, Riffat S.** Field trial of Saussurea lappa roots against nematodes and Nigella sativa seeds against cestodes in children. J Pak Med Assoc. 1991; 41:185–187. [PubMed] [Google Scholar]

[21] **Al-Attass, S.A.; Zahran, F.M.; Turkistany, S.A.** Nigella sativa and its active constituent thymoquinone in oral health. Saudi Med. J. 2016, 37, 235–244.

[22] **Ali B, Blunden G.** Pharmacological and toxicological properties of Nigella sativa [J]. Phytother Res, 2003, 17(4): 299-305.

[23] **Al Yahya M.** Phytochemical studies of the plants used in traditional medicine of Saudi Arabia [J]. Fitoterapia, 1986, 57: 179-182.

[24] **Aljabre SH, Randhawa MA, Akhtar N, Alakloby OM, Alqurashi AM, Aldossary A.** Antidermatophyte activity of ether extract of Nigella sativa and its active principle, thymoquinone. J Ethnopharm 2005; 101(1-3): 116-119.

[25] **Almaie, S., 2015.** Nigella sativa improves glycemic control and ameliorates oxidative stress in patients with type 2 diabetes mellitus: placebo controlled participant blinded clinical trial. PLoS ONE. 10, e0113486.

[26] **Al Mofleh IA, Alhaider AA, Mossa JS, et al.** Gastroprotective effect of an aqueous suspension of black cumin Nigella sativa on necrotizing agents-induced gastric injury in experimental animals [J]. Saudi J Gastroenterol, 2008, 14(3): 128-134.

[27] **Ali, B.H., Blunden, G., 2003.** Pharmacological and toxicological properties of Nigella sativa. Phytother Res. 17, 299–305. https://doi.org/10.1002/ptr.1309.

[28] **Al-Jishi, S.A.A.** A study of Nigella sativa on blood hemostatic functions. M.Sc. Thesis, King Faisal University, Dammam, Saudi Arabia, 2000.

[29] **Al-Jenoobi, F.I., Al-Thukair, A.A., Abbas, F.A., Ansari, M.J., Alkharfy, K.M., Al-Mohizea, A.M., Al-Suwayeh, S.A., Jamil, S., 2010.** Effect of black seed on dextromethorphan O- and N-demethylation in human liver microsomes and healthy human subjects. Drug Metab. Lett. 4, 51- 55.

[30] **Ait Mbarek, L., H. Ait Mouse, N. Elabbadi, M. Bensalah, A. Gamouh, R.A. Aboufatima, A.**

[31] **Benharref, A. Chait, M. Kamal, A. Dalal and A. Zyad.** Anti-tumor properties of black seed (Nigella sativa L.) extract. Braz. J. Med. Biol. Res. 40(6): 839–847, 2007.

[32] **Al-Sa'aidi JAA, Al-Khuzai ALD, Al-Zobaydi NFH.** Effect of alcoholic extract of Nigella sativa on fertility in male rats [J]. Iraqi J Vet Sci, 2009, 23: 123-128.

[33] **Al-Sheddi, E.S., Farshori, N.N., Al-Oqail, M.M., Musarrat, J., Al-Khedhairy, A.A., Siddiqui, M.A., 2014.** Cytotoxicity of Nigella sativa seed oil and extract against human lung cancer cell line. Asian Pac. J. Cancer Prev. 15, 983-987.

[34] **Amarouch H, Zaoui A, Cherrah Y, et al.** Acute and chronic toxicity of Nigella sativa fixed oil [J]. Phytomedicine, 2002, 9(1): 69-74.

[35] **Ara N, Choudhury S, Amin R.** In vitro antimicrobial activity of the volatile oil of Nigella sativa Linn seeds [J]. TAJ: J Teach Assoc, 2005, 18: 109-112.

[36] **Awad E, Binder B.** In vitro induction of endothelial cell fibrinolytic alterations by Nigella sativa [J]. Phytomedicine, 2005, 12(3): 194-202.

[37] **Ayaz E, Yilmaz H, Ozbek H, Tas Z, Orunc O (2007).** The effect of Nigella sativa oil against Aspiculuris tetraptera and Hymenolepis nana in naturally infected mice. Saudi Med. J. 28:1654-1657.

[38] **Bakathir HA, Abbas NA.** Detection of the antibacterial effect of Nigella sativa ground seedswith water [J]. Afr J Tradit Complement Altern Med, 2011, 8(2): 159-164.

[39] **Bamosa, A.O., Kaatabi, H., Lebdaa, F.M., Elq, A.M., Al-Sultanb, A., 2010.** Effect of Nigella sativa seeds on the glycemic control of patients with type 2 diabetes mellitus. Indian J. Physiol.

[40] Pharmacol. 54, 344-354.

[41] **Bhatti, I.U., Ur Rehman, F., Khan, M.A., Marwat, S.K., 2009.** Effect of prophetic medicine kalonji [Nigella sativa l.] on lipid profile of human beings. An in vivo approach. World Applied Sciences Journal. 6, 1053-1057.

[42] **Burits M, Bucar F.** Antioxidant activity of Nigella sativa essential oil. Phytother Res. 2000; 14:323–328. [PubMed] [Google Scholar]

[43] **Burits M, Bucar F.** Antioxidant activity of Nigella sativa essential oil. Phytother Res 2000; 14:323-328.

[44] **Badary OA, Bdel-Naim AB, Bdel-Wahab MH, Hamada FM.** The influence of thymoquinone on doxorubicine-induced hyperlipidemic nephropathy in rats. Toxicology 2000; 143:219-226.

[45] **Bamosa, A.O., Kaatabi, H., Lebdaa, F.M., Elq, A.M., Al-Sultanb, A., 2010.** Effect of Nigella sativa seeds on the glycemic control of patients with type 2 diabetes mellitus. Indian J. Physiol. Pharmacol. 54, 344-354.

[46] **Bin Sayeed, M.S., Shams, T., Fahim Hossain, S., Rahman, M.R., Mostofa, A., Fahim Kadir, M., Mahmood, S, Asaduzzaman, M., 2014.** Nigella sativa L. seeds modulate mood, anxiety and cognition in healthy adolescent males. J. Ethnopharmacol. 152, 156-162.

[47] **Benhaddou-Andaloussi A, Martineau L, Vuong T, et al.** The in vivo antidiabetic activity of Nigella sativa is mediated through activation of the AMPK pathway and increased muscle Glut4 content [J]. Evid Based Complement Alternat Med, 2011, 2011: 538671.

[48] **Bita A, Rosu A, Calina D, et al.** An alternative treatment for Candida infections with Nigella sativa extracts [J]. Eur J Hosp Pharm, 2012, 19: 162.

[49] **Bakathir HA, Abbas NA.** Detection of the antibacterial effect of Nigella sativa ground seeds with water. Afr J Tradit Compl Altern Med. 2011; 8:159–164. [PMC free article] [PubMed] [Google Scholar]

[50] **Baghdadi HB, Al-Mathal EM.** Anti-coccidial activity of Nigella sativa L. J Food Agricul Envir. 2011; 9:10–17. [Google Scholar]

[51] **Bita A , Rosu AF, Calina D, Rosu L, Zlatian O, Dindere C, et al.** An alternative treatment for Candida infections with Nigella sativa extracts. Eur J Hosp Pharm 2012; 19: 162.

[52] **Boskabady MH, Keyhanmanesh R, Saadatloo MA.** Relaxant effects of different fractions from Nigella sativa L. on guinea pig tracheal chains and its possible mechanism(s). Indian J Exp Biol 2008; 46(12): 805-810.

[53] **Boskabady MH, Javan H, Sajady M, Rakhshandeh H.** The possible prophylactic effect of Nigella sativa seed extract in asthmatic patients. Fundam Clin Pharmacol. 2007; 21(5):559-66.

[54] **Boskabady MH, Farhadi J.** The possible prophylactic effect of Nigella sativa seed aqueous extract on respiratory symptoms and pulmonary function tests on chemical war victims: a randomized, double-blind, placebo-controlled trial. J Altern Complement Med. 2008; 14(9):1137-44.

[55] **Boskabady, M.H., Mohsenpoor, N., Takaloo, L., 2010.** Antiasthmatic effect of Nigella sativa in airways of asthmatic patients. Phytomedicine.17, 707-713.

[56] **Chakarvarti N (1993).** Inhibition of histamine release from mast cells by nigellone. Ann. Allergy. 70(3):237-242.

[57] **Chevallier A (1996).** Encyclopedia of medicinal plants. New York, NY: DK Publishing. p. 237.

[58] **Daba MH, Abdel-Rehman MS (1998).** Hepatoprotective activity of thymoquinone in isolated rat hepatocytes. Toxicol. Lett. 95:23-29.

[59] **Dehkordi, F.R., Kamkhah, A.F., 2008.** Antihypertensive effect of Nigella sativa seed extract in patients with mild hypertension. Fundam. Clin. Pharmacol. 22, 447-452.

[60] **Dorman HJ, Deans SG.** Antimicrobial agents from plants: antibacterial activity of plant volatile oils. J Appl Microbiol. 2000; 88:308–316. [PubMed] [Google Scholar]

[61] **Dorucu M, Colak SO, Ispir U, et al.** The effect of black cumin seeds, Nigella sativa, on the immune response of rainbow trout, Oncorhynchus mykiss [J]. Med Aquacult J, 2009, 2: 1-7.

[62] **Durmus AS, Ceribasi S, Yaman M.** Effects of Nigella sativa and silver sulfadiazine on burn wound healing in rats [J]. Vet Med, 2010, 55(12): 619-624.

[63] **El-Abhar H, Abdallah D, Saleh S.** Gastroprotective activity of Nigella sativa oil and its constituent, thymoquinone, against gastric

mucosal injury induced by ischaemia/reperfusion in rats [J]. J Ethnopharmacol, 2003, 84(2-3): 251-258.

[64] **El-Dakhakhny M, Barakat M, Abd El-Halim M, et al.** Effects of Nigella sativa oil on gastric secretion and ethanol induced ulcer in rats [J]. J Ethnopharmacol, 2000, 72(1-2): 299-304.

[65] **El-Kadi, A. and O. Kandil.** Effect of Nigella sativa (the black seed) on immunity. In: Proceedings of the Fourth International Conference on Islamic Medicine, 4 November, Kuwait, 1986, pp. 344–348.

[66] **El Kadi , A., Kandil, O., Tabuni, A.M., 1990.** Nigella sativa and cell mediated immunity. Arch. AIDS Res. 1, 232-234.

[67] **El-Hadi MA, Bakri YM, Yousif G (2010).** Mohammed and Hassan S. Khalid. Antiplasmodial Activity of Some Medicinal Plants Used in Sudanese Folk-medicine. Environ. Health Insights. 4:1-6.

[68] **El-Tahir K E H, Bakeet DM.** The black seed Nigella sativa L. a min for multi cure: a plea for urgent clinical evaluation of its volatile oil. J Taibah Uni Med Sci 2006; 1: 1-19.

[69] **El-Tawil O, Moussa SZ.** Antioxidant and hepatoprotective effects of thymoquinone against carbon tetrachloride-induced hepatotoxicity in isolated rat hepatocyte. J Egypt Soc Toxicol 2006; 34:33-41.

[70] **ElShenawy NS, Soliman MF, Reyad SI (2008).** The effect of antioxidant properties of aqueous garlic extract and Nigella sativa as anti-schistosomiasis agents in mice. Rev. Inst. Med. Trop. 50:29-36.

[71] **El-Tawil O, Moussa SZ.** Antioxidant and hepatoprotective effects of thymoquinone against carbon tetrachloride-induced hepatotoxicity in isolated rat hepatocyte. J Egypt Soc Toxicol 2006; 34:33-41.

[72] **El-Tahir KE, Ashour M, Al-Harbi MM (1993).** The respiratory effects of the volatile oil of black seed (Nigella sativa) in guinea pigs: elucidation of the mechanism(s) of action. Gen. Pharmacol. 24(5):1115-1122.

[73] **El-Tahir KE, Ashour MM, Al-Harbi MM (1993).** The cardiovascular effects of the volatile oil of black seed (Nigella sativa) in

rats: elucidation of the mechanism(s) of action. Gen. Pharmacol. 24(5):1123-1131.

[74] **Enomoto S, Asano R, Iwahori Y, Narui T, Okada Y, Singab AN, et al.** Hematological studies on black cumin oil from the seeds of Nigella sativa L. Biol Pharm Bull. 2001; 24:307–310. [PubMed] [Google Scholar]

[75] **Farah, I.O. and R.A. Begum.** Effect of Nigella sativa (N. sativa L.) and oxidative stress on survival pattern of MCF-7 breast cancer cells. Biomed. Sci. Instrum. 39: 359–364, 2003.

[76] **Fararh K, Atoji Y, Shimizu Y, et al.** Mechanisms of the hypoglycemic and immunopotentiating effects of Nigella sativa L. oil in streptozotocin-induced diabetic hamsters [J]. Res Vet Sci, 2004, 77(2):123-129.

[77] **Fahrettin Y, Sacit C, Alpaslan T, Mustafa A, Nurten A, Hale C, Ali RO, Muharrem B (2008).** Nigella sativa relieves the deleterious effects of ischemia reperfusion injury on liver. World J. Gastroenterol. 14(33):5204-5209.

[78] **Fallah Huseini, H., Amini, M., Mohtashami, R., Ghamarchehre, M.E., Sadeqhi, Z., Kianbakht, S., Fallah Huseini, A., 2013.** Blood pressure lowering effect of Nigella sativa L. seed oil in healthy volunteers: a randomized, double-blind, placebo-controlled clinical trial. Phytother. Res. 27, 1849- 1853.

[79] **Fouda AMM, Daba MHY, Yousef Ahmed AR.** Antigenotoxic effects of thymoquinone against benzo[a]pyrene and mitomycin C -induced genotoxicity in cultured human lymphocytes. Research in Immunology: An International Journal 2014; 2014: Articl ID 5352.79.

[80] **Gali-Muhtasib, H., Diab-Assaf, M., Boltze, C., Al-Hmaira, J., Hartig, R., Roessner, A., Schneider- Stock, R., 2004.** Thymoquinone extracted from black seed triggers apoptotic cell death in human colorectal cancer cells via a p53-dependent mechanism. Int. J. Oncol. 25, 857-866.

[81] **Ghaznavi KM (1991).** Tibbe-e-Nabvi aur Jadid Science, Al-Faisal Nasheeran wa Tajeera-e- Kutab. Urdu Bazar Lahore, Pakistan. 1:228-236.

[82] **Gharibi D, Ghorbanpoor Najafabadi NM, Mohabat A.** Study of antibacterial activity of ethanol extract from Nigella sativa against some important veterinary bacterial pathogens [J]. J Vet Microbiol, 2012, 8: 13-21.

[83] **Gheita, T.A., Kenawy, S.A., 2012.** Effectiveness of Nigella sativa oil in the management of rheumatoid arthritis patients: a placebo controlled study. Phytother. Res. 26, 1246-1248.

[84] **Gholamnezhad Z, Havakhah S, Boskabady MH.** Preclinical and clinical effects of Nigella sativa and its constituent, thymoquinone: a review. J Ethnopharmacol. 2016; 190:372–86.

[85] **Gholamnezhad Z, Boskabady MH, Hosseini M.** Effect of Nigella sativa on immune response in treadmill exercised rat [J]. BMC Complement Altern Med, 2014, 14: 437.

[86] **Ghoneim MT, El-Gindy AR, El-Alami R, Shoukry E, Yaseen S (1982).** Possible effects of some extracts of Nigella sativa L seeds on blood coagulation system and fibrinolytic activity. Proceeding of 2nd International Conference on Islamic Medicine 12th Apr, Kuwait. pp. 528-535.

[87] **Ghonime M, Eldomany R, Abdelaziz A, et al.** Evaluation of immunomodulatory effect of three herbal plants growing in Egypt [J]. Immunopharmacol Immunotoxicol, 2011, 33(1): 141-145.

[88] **Ghorbanibirgani, A., Khalili, A., Rokhafrooz, D., 2014.** Comparing Nigella sativa Oil and Fish Oil in Treatment of Vitiligo. Iran. Red. Crescent. Med. J.16, e4515.

[89] **Goel, S.; Mishra, P.** Thymoquinone inhibits biofilm formation and has selective antibacterial activity due to ROS generation. Appl. Microbiol. Biotechnol. 2018, 102, 1955–1967. [CrossRef]

[90] **Gokce A, Oktar S, K oc A, Yonden Z.** Protective effects of thymoquinone against methotrexate- induced testicular injury. Hum Exp Toxicol 2011; 30(8): 897-903.

[91] **Goyal, S.N.; Prajapati, C.P.; Gore, P.R.; Patil, C.R.; Mahajan, U.B.; Sharma, C.; Talla, S.P.; Ojha, S.K.** Therapeutic Potential and Pharmaceutical Development of Thymoquinone: A Multitargeted Molecule of Natural Origin. Front. Pharmacol. 2017, 8. [CrossRef]

[92] **Hadjzadeh MA, Keshavarzi Z, Yazdi TSA, Ghasem SM, Rajaei Z, Khajavi Rad A.** Effect of alcoholic extract of Nigella sativa on cisplatin-induced toxicity in rat. Iran J Kidney Dis 2012; 6(2): 99-104.

[93] **Hagag, A.A., Elaal, A.M.A., Elsheik, A., Elzamarany, E.A., 2013.** Protective effect of Nigella sativa oil against methotrexate induced hepatotoxicity in children with acute lymphoblastic leukemia. J. Leuk. 1, 123.

[94] **Halamova K, Kokoska L, Flesar J, Sklenickova O, Svobodova B, Marsik P.** In vitro antifungal effect of black cumin seed quinones against dairy spoilage yeasts at different acidity levels. J Food Prot 2010; 73(12): 2291-2295.

[95] **Hamid M. and Hossein H. (2014).** The protective effect of Nigella sativa against liver injury: a review. Iran J Basic Med Sci 2014; 17:958-966.

[96] **Hanafy M, Hatem M.** Studies on the antimicrobial activity of Nigella sativa seed (black cumin) [J]. J Ethnopharmacol, 1991, 34(2-3): 275-278.

[97] **Hanafy MS, Hatem ME.** Studies on the antimicrobial activity of Nigella sativa seed (black cumin) J Ethnopharmacol. 1991; 34:275–278. [PubMed] [Google Scholar]

[98] **Hannan A, Saleem S, Chaudhary S, Barkaat M, Arshad MU.** Anti-bacterial activity of Nigella sativa against clinical isolates of methicillin resistant Staphylococcus aureus. J Ayub Med Coll Abbottabad. 2008; 20:72–74. [PubMed] [Google Scholar]

[99] **Haq A, Abdullatif M, Lobo PI, Khabar KS, Sheth KV, Al-Sedairy ST (1995).** Nigella sativa: Effect on human lympocytes and

polymorphonuclear leucocyte phagocytic activity. Immunopharmacol. 30(2):147-155.

[100] **Haq, A., Lobo, P.I., Al-Tufail, M., Rama, N.R., Al-Sedairy, S.T., 1999.** Immunomodulatory effect of Nigella sativa proteins fractionated by ion exchange chromatography. Int. J. Immunopharmacol. 21, 283-295.

[101] **Haque, S.F., Nasiruddin, M., Najmi, A., 2011.** Indigenous herbal product Nigella sativa proved effective as an anti-obesity therapy in metabolic syndrome. International Journal of Medicobiological Res. 1, 133 - 176.

[102] **Heshmati J, Namazi N, Memarzadeh MR, Taghizadeh M, Kolandooz F.** Nigella sativa oil affects glucose metabolism and lipid concentrations in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled trial. Food Res Int. 2015; 70:87-93.

[103] **Heshmati, J. and Namazi, N., 2015.** Effects of black seed (Nigella sativa) on metabolic parameters in diabetes mellitus: a systematic review. Complement. Ther. Med. 23, 275-282.

[104] **Hosseinzadeh H, Fazly Bazzaz BS, Haghi MM.** Antibacterial activity of total extracts and essential oil of Nigella sativa L. seeds in mice. Pharmacologyonline 2007; 2:429-435.

[105] **Hossein BM, Nasim V, Sediqa A.** The protective effect of Nigella sativa on lung injury of sulfur mustard-exposed Guinea pigs. Exp Lung Res 2008; 34(4): 183-194.

[106] **Hosseini M, Zakeri S, Khoshdast S, et al.** The effects of Nigella sativa hydro-alcoholic extract and thymoquinone on lipopolysaccharide-induced depression like behavior in rats [J]. J Pharm Bioallied Sci, 2012, 4(3): 219-225.

[107] **Hosseini, M.S., Mirkarimi, S.A., Amini, M., Mohtashami, R., Kianbakht, S., Fallah Huseini, H., 2013.** Effects of Nigella sativa L. seed oil in type II diabetic patients: a randomized, double-blind, placebo - controlled clinical trial. Journal of Medicinal Plants. 12, 93-99.

[108] **Houcher Z, Boudiaf K, Benboubetra M, et al.** Effects of methanolic extract and commercial oil of Nigella sativa L. on blood glucose and antioxidant capacity in alloxan-induced diabetic rats [J]. Pteridines, 2007, 18: 8-18.

[109] **Hosseinzadeh H, Parvardeh S (2004).** "Anticonvulsant effects of thymoquinone, the major constituent of Nigella sativa seeds, in mice." Phytomed. 11(1):56-64.

[110] **Hosseinzadeh H, Parvardeh S, Nassiri-Asl M, and Mansouri MT (2005),** "Intracerebroventricular administration of thymoquinone, the major constituent of Nigella sativa seeds, suppresses epileptic seizures in rats," Med. Sci. Monitor 11(4):106-110.

[111] **Ibrahim, R.M., Hamdan, N.S., Mahmud, R., Imam, M.U., Saini, S.M., Rashid, S.N., Abd Ghafar, S.A., Latiff, L.A., Ismail, M., 2014b.** A randomised controlled trial on hypolipidemic effects of Nigella Sativa seeds powder in menopausal women. J. Transl. Med. 12, 82.

[112] **Isik, H ,.Cevikbas, A., Gurer, U.S., Kiran, B., Uresin, Y., Rayaman, P., Rayaman, E., Gurbuz, B., Buyukozturk, S., 2010.** Potential adjuvant effects of Nigella sativa seeds to improve specific immunotherapy in allergic rhinitis patients. Med. Princ. Pract. 19, 206-211.

[113] **Islam, S.N., P. Begum, T. Ahsan, S. Huque and M. Ahsan.** Immunosuppressive and cytotoxic properties of Nigella sativa. Phytother. Res. 18(5): 395–398, 2004.

[114] **Jrah Harzallah H, Grayaa R, Kharoubi W, et al.** Thymoquinone, the Nigella sativa bioactive compound, prevents circulatory oxidative stress caused by 1, 2-dimethylhydrazine in erythrocyte during colon postinitiation carcinogenesis [J]. Oxid Med Cell Longev, 2012, 2012: 854065.

[115] **Kaatabi, H., Bamosa, A.O., Badar, A., Al-Elq, A., Abou-Hozaifa, B., Lebda, F., Al-Khadra, A., Al-**

[116] **Kalus, U., Pruss, A., Bystron, J., Jurecka, M., Smekalova, A., Lichius, J.J., Kiesewetter, H., 2003.**

[117] Effect of Nigella sativa (black seed) on subjective feeling in patients with allergic diseases. Phytother. Res. 17, 1209-1214.

[118] **Kamil ZH.** Spectacular black seeds (Nigella sativa): Medical importance review [J]. Med J Babylon, 2013, 10(4): 1-9.

[119] **Kanter M, Meral I, Yener Z, et al.** Partial regeneration/ proliferation of the beta-cells in the islets of langerhans by Nigella sativa L. in streptozotocin-induced diabetic rats [J]. Tohoku J Exp Med, 2003, 201(4): 213-219.

[120] **Kanter M.** Effects of Nigella sativa seed extract on ameliorating lung tissue damage in rats after experimental pulmonary aspirations. Acta Histochem 2009; 111(5): 393-403.

[121] **Kapil, H.; Suresh, D.K.; Bathla, S.C.; Arora, K.S.** Assessment of clinical efficacy of locally delivered 0.2% Thymoquinone gel in the treatment of periodontitis. Saudi Dent. J. 2018, 30, 348–354. [CrossRef]

[122] **Kapoor S.** Emerging clinical and therapeutic applications of Nigella sativa in gastroenterology. World J Gastroenterol 2009; 7: 2170-2171.

[123] **Kardani, A.K., Fitri, L.E., Barlianto, W., Olivianto, E., Kusuma, H.M.S.C., 2013.** The Effect of House Dust Mite Immunotherapy, Probiotic and Nigella sativa in The Number of Th17 Cell and Asthma Control Test Score. IOSR-JDMS. 6, 37-47.

[124] **Keshri G, Singh MM, L akshmi V, Kamboj VP.** Post-coital contraceptive efficacy of the seeds of Nigella sativa in rats. Indian J Physiol Pharm 1995; 39(1): 59-62.

[125] **Khaled A, Abdel-Sater (2009).** Gastroprotective effects of Nigella sativa oil on the formation of stress gastritis in hypothyroidal rats. Int. J. Physiol. Pathophysiol. Pharmacol. 1:143-149.

[126] **Khanna T, Zaidi FA, Dandiya PC (1993).** CNS and analgesic studies of Nigella sativa. Fitoterapia. 5:407-410.

[127] **Kiari, F.Z.; Meddah, B.; Tir Touil Meddah, A.** In vitro study on the activity of essential oil and methanolic extract from Algerian Nigella sativa L. Seeds on the growth kinetics of microorganisms isolated from the

buccal cavities of periodontal patients. Saudi Dent. J. 2018, 30, 312–323. [CrossRef] [PubMed]

[128] **Kolahdooz, M., Nasri, S., Modarres, S.Z., Kianbakht, S., Huseini, H.F., 2014.** Effects of Nigella sativa L. seed oil on abnormal semen quality in infertile men: a randomized, double-blind, placebo-controlled clinical trial. Phytomedicine. 21, 901-905.

[129] **Kooti W, Hasanzadeh-Noohi Z, Sharafi-Ahvazi N, et al.** Phytochemistry, pharmacology, and therapeutic uses of black seed (Nigella sativa). Chin J Nat Med 2016; 14(10):732-45.

[130] **Kruk I, Michalska T, Klanda A (2000).** The effect of thymol and its derivatives on reaction generating reactive oxygen species. Chemosphere. 41:1059-1064.

[131] **Latiff, L.A., Parhizkar, S., Dollah, M.A., Hassan, S.T., 2014.** Alternative supplement for enhancement of reproductive health and metabolic profile among perimenopausal women: a novel role of Nigella sativa. Iran. J. Basic Med. Sci. 17, 980-985.

[132] **Mabrouk, G.M., S.S. Moselhy, S.F. Zohny, E.M. Ali, T.E. Helal, A.A. Amin and A.A. Khalifa.**

[133] Inhibition of methylnitrosourea (MNU) induced oxidative stress and carcinogenesis by orally administered honey and Nigella sativa in Sprague Dawley rats. J. Exp. Clin. Cancer Res. 21(3): 341–346, 2002.

[134] **Mahgoub AA.** Thymoquinone protects against experimental colitis in rats. Toxicol Lett 2003; 143:133-143.

[135] **Mahmoud M, El-Abhar H, Saleh S.** The effect of Nigella sativa oil against the liver damage induced by Schistosoma mansoni infection in mice [J]. J Ethnopharmacol, 2002, 79(1): 1-11.

[136] **Mahmoud MR, El-Abhar HS, Salh S (2002).** The effect of Nigella sativa oil against the liver damage induced by Schistosoma mansoni infection in mice. J. Ethnopharmacol. 79(1):1-11.

[137] **Mahmoud, S.S., Torchilin, V.P., 2013.** Hormetic/cytotoxic effects of Nigella sativa seed alcoholic and aqueous extracts on MCF-7 breast

cancer cells alone or in combination with doxorubicin. Cell Biochem. Biophys. 66, 451-460

[138] **Maideen, N.M.P.** Prophetic Medicine-Nigella Sativa (Black cumin seeds) - Potential herb for COVID-19? J. Pharmacopuncture 2020, 23, 62–70. [CrossRef] [PubMed]

[139] **Majdalawieh AF, Fayyad MW.** Immunomodulatory and anti-inflammatory action of Nigella sativa and thymoquinone: a comprehensive review. Int Immunopharmacol. 2015; 28(1):295–304.

[140] **Majdalawieh, A.F., R. Hmaidan and R.I. Carr.** Nigella sativa modulates splenocyte proliferation,

[141] Th1/Th2 cytokine profile, macrophage function and NK anti-tumor activity. J. Ethno-pharmacol. 131(2): 268–275, 2010.

[142] **Mansour M, Tornhamre S.** Inhibition of 5 lipoxygenase and leukotriene C4 synthase in human blood cells by thymoquinone. J Enzyme Inhib Med Chem 2004; 19:431-436.

[143] **Mat, M.C., Mohamed, A.S., Hamid, S.S., 2011.** Primary human monocyte differentiation regulated by Nigella sativa pressed oil. Lipids Health. Dis. 10, 216.

[144] **Memon, A.R., Shah, S.S., Memon, A.R., Naqvi, S.H.R., 2012.** Effect of combination of Nigella sativa and Trigonella foenum-graecum with glibenclamide on serum triglycerides, HDL, and creatinine levels in type 2 diabetes mellitus patients. Pakistan Journal of Pharmacology 29, 1-6.

[145] **Merfort I, Wray V, Barakat HH, Hussein SAM, Nawwar MAM, Willuhn G.** Flavonoid triglycerides from seeds of Nigella sativa. Phytochemistry. 1997; 46:359–363. [Google Scholar]

[146] **Meral I, Donmez N, Baydas B, et al.** Effect of Nigella sativa L. on heart rate and some haematological values of alloxan-induced diabetic rabbits [J]. Scand J Lab Anim Sci, 2004, 31: 49-53.

[147] **Mohamed A, Afridi DM, Garani O, Tucci M.** Thymoquinone inhibites the activation of NF-kappaB in the brain and spinal cord of

experimental autoimmune encephalomyelitis. Biomed Sci Instrum 2005; 41:388-393.

[148] **Mohamed Mekhemar, Yasmine Hassan and Christof Dörfer (2020):** Nigella sativa and Thymoquinone: A Natural Blessing for Periodontal Therapy. Antioxidants 2020, 9, 1260; doi:10.3390/antiox9121260.

[149] **Mohtashami R, Huseini HF, Heydari M, Amini M, Sadeqhi Z, Ghaznavi H, et al.** Efficacy and safety of honey based formulation of Nigella sativa seed oil in functional dyspepsia: a double blind randomized controlled clinical trial. J Ethnopharmacol. 2015; 175:147-52.

[150] **Monika T, Sasikala P, Vijaya Bhaskara Reddy M.** An investigational of antibacterial activities of Nigella sativa on mastaitis in dairy crossbred cows. Int J Adv Technical Res. 2013; 3:263–272. [Google Scholar]

[151] **Morsi NM.** Antimicrobial effect of crude extracts of Nigella sativa on multiple antibiotics-resistant bacteria [J]. Acta Microbiol Pol, 2000, 49(1): 63-74.

[152] **Mukhallad AM, Mohamad MJ, Mohamad P, Hatham D (2009).** Effects of Black Seeds (Nigella sativa) on Spermatogenesis and Fertility of Male Albino Rats. Res. J. Med. Med. Sci. 4(2):386-390.

[153] **Nagi MN, Mansour MA.** Protective effect of thymoquinone against doxorubicin-induced cardiotoxicity in rats: a possible mechanism of protection. Pharmacol Res 2000; 41:283-289.

[154] **New Delhi:** 1989. The Ayurvedic Pharmacopoeia of India, part 1, Ministry of Health and Family Welfare; pp. 119–120. [Google Scholar]

[155] **Najmi A, Nasiruddin M, Khan RA, Haque SF (2008).** Effect of Nigella sativa oil on various clinical and biochemical parameters of insulin resistance syndrome. Int. J. Diab. Dev. Ctries. 28:11-14.

[156] **Najmi, A., Nasiruddin, M., Khan, R.A., Haque, S.F., 2012.** Therapeutic effect of Nigella Sativa in patients of poor glycemic control. Asian Journal of Pharmaceutical and Clinical 5, 224-228.

[157] **Nadia MH, Taha RA (2009).** Effects of Nigella sativa Oil and Thymoquinone on Oxidative Stress and Neuropathy in Streptozotocin-Induced Diabetic Rats. Pharmacology 84:127-134.

[158] **Namjoo A, Sadri SM, Rafieian M, et al.** Comparing the effects of Nigella sativa extract and gentamicin in treatment of urinary tract infection caused by Ecoli [J]. J Mazandaran Univ Med Sci, 2013, 22: 22-29.

[159] **Niakan M, Miri SRA, Naseri M, et al.** In vitro anti-staphylococcus aureus activity of Nigella sativa L. seed oil extract, compared with CXM, CEC, MAN and CAZ antibiotics [J]. J Med Plants, 2006, 3: 29-33.

[160] **Nikakhlagh, S., Rahim, F., Aryani, F.H.N., Syahpoush, A., Brougerdnya, M.G., Saki, N., 2011.**

[161] Herbal treatment of allergic rhinitis: the use of Nigella sativa. American Journal of Otolaryngology 32, 402-407.

[162] **Nair MKM, Vasudevan P, Venkitanarayanan K.** Antibacterial effect of black seed oil on Listeria monocytogenes. Food Cont. 2005; 16:395–398. [Google Scholar]

[163] **Nemmar A, AlSalam S, Zia S, et al.** Contrasting actions of diesel exhaust particles on the pulmonary and cardiovascular systems and the effects of thymoquinone [J]. Br J Pharmacol, 2011, 164(7): 1871-1882.

[164] **Nagi MN, Alam K, Badary OA, Al-Shabanah OA, Al-Sawaf HA, AL- Bekairy AM (1999).** Thymoquinone protects against carbon tetracholide hepatotoxicity in mice via an antioxidant mechanism. Biochem. Mol. Biol. Int. 47:153-159.

[165] **Ng, W.K., Yazan, L.S., Ismail, M., 2011.** Thymoquinone from Nigella sativa was more potent than cisplatin in eliminating of SiHa cells via apoptosis with down-regulation of Bcl-2 protein. Toxicol. In Vitro. 25, 1392-1398.

[166] **Ng Cho Ping, Hashim NH, Hasan Adli DS.** Effects of Nigella sativa (Habbatus sauda) oil and nicotine chronic treatments on sperm parameters and testis histological features of rats [J]. Evid Based Complement Alternat Med, 2014, 2014: 218293.

[167] **Okeola VO, Adaramoye OA, Nneji CM, Falade CO, Farombi EO, Ademowo OG.** Antimalarial and antioxidant activities of methanolic extract of Nigella sativa seeds (black cumin) in mice infected with Plasmodium yoelli nigeriensis. Parasitol Res. 2011; 108:1507–1512. [PubMed] [Google Scholar]

[168] **Osama A. Abu-Zinadah.** Using Nigella sativa oil to treat and heal chemical induced wound of rabbit skin [J]. JKAU: Sci, 2009, 21(2): 335-346.

[169] **Parvardeh S, Nassiri-Asl M, Mansouri M, et al.** Study on the anticonvulsant activity of thymoquinone, the major constituent of Nigella sativa L. seeds, through intracerebroventricular injection [J]. J Med Plants, 2005, 2: 45-52.

[170] **Pari L, Sankaranarayanan C.** Beneficial effects of thymoquinone on hepatic key enzymes in streptozotocin– nicotinamide induced diabetic rats [J]. Life Sci, 2009, 85(23-26): 830-834.

[171] **Peterhans E.** Oxidants and antioxidants in viral diseases: disease mechanisms and metabolic regulation. J Nutr. 1997; 127:962S–965S. [PubMed] [Google Scholar]

[172] **Perveen T, Haider S, Kanwal S, Haleem DJ (2009).** "Repeated administration of Nigella sativa decreases 5-HT turnover and produces anxiolytic effects in rats," Pak. J. Pharm. Sci. 22(2):139- 144.

[173] Phillips JD. Medicinal plants. Biologist. 1992; 39:187–191. [Google Scholar]

[174] **Peng, L., Liu, A., Shen, Y., Xu, H.Z., Yang, S.Z., Ying, X.Z., Liao, W., Liu, H.X., Lin, Z.Q., Chen, Q.Y., Cheng, S.W., Shen, W.D., 2013.** Antitumor and anti-angiogenesis effects of thymoquinone on osteosarcoma through the NF-kappaB pathway. Oncol. Rep. 29, 571-578.

[175] **Qidwai, W., Hamza, H.B., Qureshi, R., Gilani, A., 2009.** Effectiveness, safety, and tolerability of powdered Nigella sativa (kalonji) seed in capsules on serum lipid levels, blood sugar, blood pressure, and

body weight in adults: results of a randomized, double-blind controlled trial. J. Altern. Complement. Med. 15, 639-644.

[176] **Rajsekhar S, Kuldeep B.** Pharmacognosy and pharmacology of Nigella sativa. J Pharm Res. 2011; 2:36–39. [Google Scholar]

[177] **Rajkapoor B, Anandan R, Jayakar B (1996).** Anti-ulcer effect of Nigella sativa and Pongamia pannata in rats. Fitoterapia. 67:195-199.

[178] **Ramadan MF, Kroh LW, Mörsel JT.** Radical scavenging activity of black cumin (Nigella sativa L.), coriander (Coriandrum sativum L.), and niger (Guizotia abyssinica Cass.) crude seed oils and oil fractions [J]. J Agric Food Chem, 2003, 51(24): 6961-6969.

[179] **Roepke, M., Diestel, A., Bajbouj, K., Walluscheck, D., Schonfeld, P., Roessner, A., Schneider-Stock, R., Gali-Muhtasib, H., 2007.** Lack of p53 augments thymoquinone-induced apoptosis and caspase activation in human osteosarcoma cells. Cancer Biol. Ther. 6, 160-169.

[180] **Rogozhin EA, Oshchepkova YI, Odintsova TI, Khadeeva NV, Veshkurova ON, Egorov TA, et al.** Novel antifungal defensins from Nigella sativa L. seeds. Plant Physiol Biochem. 2011; 49:131–137. [PubMed] [Google Scholar]

[181] **Roughani M, Vaez MM, Vaseei M.** The effect of long-term oral administration of Nigella sativum on the contractile reactivity of thoracic aorta in diabetic rats [J]. Koomesh, 2006, 7(3-4): 153-157.

[182] **Sabzghabaee, A.M., Dianatkhah, M., Sarrafzadegan, N., Asgary, S., Ghannadi, A., 2012.** Clinical evaluation of Nigella sativa seeds for the treatment of hyperlipidemia: a randomized, placebo controlled clinical trial. Med. Arch. 66, 198-200.

[183] **Salem, M.L., 2005.** Immunomodulatory and therapeutic properties of the Nigella sativa L. seed. Int. Immunopharm. 5, 1749–1770. https://doi.org/10.1016/j.intimp.2005.06.008.

[184] **Salem ML, Hossain MS.** Protective effect of black seed oil from Nigella sativa against murine cytomegalovirus infection. Int J Immunopharmacol. 2000; 22:729–740. [PubMed] [Google Scholar]

[185] **Salem EM, Yar T, Bamosa AO, Al-Quorain A, Yasawy MI, Alsulaiman RM, Randhawa MA (2010).** Comparative study of Nigella sativa and triple therapy in eradication of Helicobacter Pylori in patients with non-ulcer dyspepsia. Saudi J. Gastroenterol. 16:207-214.

[186] **Saleem U, Ahmad B, Rehman K, Mahmood S, Alam M, Erum A.** Nephro-protective effect of vitamin C and Nigella sativa oil on gentamicin associated nephrotoxicity in rabbits. Pak J Pharm Sci 2012; 25(4): 727-730.

[187] **Saleem U, Ahmad B, Rehman K, et al.** Nephro-protective effect of vitamin C and Nigella sativa oil on gentamicin associated nephrotoxicity in rabbits [J]. Pak J Pharm Sci, 2012, 25(4): 727-730.

[188] **Salomi NJ, Nair SC, Jayawardhanan KK, Varghese CD, Panikkar KR (1992).** Antitumour principles from Nigella sativa seeds. Cancer Lett. 63(1):41-46.

[189] **Salim, E.I. and S. Fukushima.** Chemopreventive potencial of volatile oil from black cumin (Nigella sativa L.) seed against rat colon carcinogenesis. Nutr. Cancer 45(2): 195–202, 2003.

[190] **Samarakoon, S.R., I. Thabrew, P.B. Galhena, D. De-Silva and K.H. Tennekoon.** A comparison of the cytotoxic potential of standardized aqueous and ethanolic extracts of a polyherbal mixture comprised of Nigella sativa (seeds), Hemidesmus indicus (roots) and Smilax glabra (rhizome). Pharmacognosy Res. 2: 335–342, 2010.

[191] **Sayed-Ahmed MM, Aleisa AM, Al-Rejaie SS, Al- Yahya AA, Al-Shabanah OA, Hafez MM, et al.** Thymoquinone attenuates diethylnitrosamine induction of hepatic carcinogenesis through antioxidant signaling. Oxid Med Cell Longev 2010; 3:254-261.

[192] **Sayed MD.** Traditional medicine in health care, J. Ethnopharmacol. 1980; 2:19–22. [PubMed] [Google Scholar]

[193] **Seronello S, Sheikh MY, Choi J.** Redox regulation of hepatitis C in nonalcoholic and alcoholic liver. Free Radic Biol Med 2007; 43:869–882.

[194] **Shabana, A., El-Menyar, A., Asim, M., Al-Azzeh, H., Al Thani, H., 2013.** Cardiovascular benefits of black cumin (Nigella sativa). Cardiovasc. Toxicol. 13, 9-21.

[195] **Sharma N. K., Ahirwar D., Jhade D. and Gupta S. (2009):** Medicinal and Phamacological Potential of Nigella sativa: A Review, Ethnobotanical Review 13: 946-55.

[196] **Shahraki, S., Khajavirad, A., Shafei, M.N., Mahmoudi, M., Tabasi, N.S. 2015.** Effect of total hydroalcholic extract of Nigella sativa and its n-hexane and ethyl acetate fractions on ACHN and GP-293 cell lines. Journal of Traditional and Complementary Medicine. 1-8.

[197] **Shawki, M., El Wakeel, L., Shatla, R., El-Saeed, G., Ibrahim, S., Badary, O., 2013.** The clinical outcome of adjuvant therapy with black seed oil on intractable paediatric seizures: a pilot study. Epileptic Disord. 15, 295-301.

[198] **Shenawy E, Nahla S, Soliman MF, et al.** The effect of antioxidant properties of aqueous garlic extract and Nigella sativa as anti-schistosomiasis agents in mice [J]. Rev Inst Med Trop Sao Paulo, 2008, 50(1): 29-36.

[199] **Shomar, B.** Major and trace elements in Nigella sativa provide a potential mechanism for its healing effects. J. Med. Plants Res. 2012, 6. [CrossRef]

[200] **Staphylakis PK, Gegiou D.** The sterols of Nigella sativa seed oil. Phytochemistry. 1986; 25:761–763. [Google Scholar]

[201] **Susanti, N., Barlianto, W., Kalim, H., Kusuma, H.M.S.C., 2013.** Asthma Clinical Improvement and Reduction in The Number of CD4+CD25+foxp3+Treg and CD4+IL-10+Cells After Administration of Immunotherapy House Dust Mite and Adjuvant Probiotics and/ or Nigella Sativa Powder in Mild Asthmatic Children. IOSR-JDMS. 7, 50-59.

[202] **Swamy, S.M. and B.K. Tan.** Cytotoxic and immunopotenciating effects of ethanolic extract of

[203] Nigella sativa L. seed. J. Ethnopharmacol. 70(1): 1–7, 2000.

[204] **Swamy S, Tan B.** Cytotoxic and immunopotentiating effects of ethanolic extract of Nigella sativa L. seeds [J]. J Ethnopharmacol, 2000, 70(1): 1-7.

[205] **Tarek El-Naggar, Mar´ıa Pilar G´omez-Serranillos, OlgaMar´ıa P, Carmen A, Mar´ıa EC (2010).** Nigella sativa L. Seed Extract Modulates the Neurotransmitter Amino Acids Release in Cultured Neurons in Vitro. J. Biomed. Biotechnol. 2010:398312.

[206] **Tekeoglu I, Dogan A, Ediz L, Budancamanak M, Demirel A.** Effects of thymoquinone (volatile oil of black cumin) on rheumatoid arthritis in rat models. Phytother Res 2007; 21:895-897.

[207] **Tembhurne SV, Feroz S, Sakarkar DM.** A review on therapeutic potential of Nigella sativa (kalonji) seeds. J Med Plants Res. 2014; 8:166–167. [Google Scholar]

[208] **Tembhurne SV, Feroz S, More B H, and Sakarkar DM.** A review on therapeutic potential of Nigella sativa (kalonji) seeds. J Med Plants Res. 2011; Vol. 8(3), pp. 167-177.

[209] **Toama MA, El-Alfy TS, El-Fatatry HM.** Antimicrobial activity of the volatile oil of Nigella sativa Linneaus seeds [J]. Antimicrob Agents Chemother, 1974, 6(2): 225-226.

[210] **Umar S, Zargan J, Umar K, et al.** Modulation of the oxidative stress and inflammatory cytokine response by thymoquinone in the collagen induced arthritis in Wistar rats [J]. Chem Biol Interact, 2012, 197(1): 40-46.

[211] **Uz E, Bayrak O, Uz E, Kaya A, Bayrak R, Uz B, et al.** Nigella sativa oil for prevention of chronic cyclosporine nephrotoxicity:an experimental model. Am J Nephrol 2008; 28(3): 517-522.

[212] **Warrier PK, Nambiar VPK, Ramankutty C, Vasudevan Nair R.** Telangana: Orient Longman; 2004. Indian Medicinal Plants: A Compendium of 500 Species; pp. 139–142. [Google Scholar]

[213] **Winkler, C., Schroecksnadel, K., Ledochowski, M., Schennach, H., Houcher, B., Fuchs, D., 2008.** In vitro Effects of Nigella sativa Seeds Extracts on Stimulated Peripheral Blood Mononuclear Cells. Pteridines. 19, 101-106.

[214] **Wienkotter N, H öpner D, SchütteU, BauerK, Begrow F, El-Dakhakhny M, et al.** The effect of nigellone & thymoquinone on inhibiting trachea contraction and mucociliary clearance. Plant Med; 2008; 74(2): 105-108.

[215] **Worthen, D.R., O.A. Ghosheh and P.A. Crooks.** The in vitro anti-tumor activity of some crude and purified components of black seed, Nigella sativa L. Anticancer Res. 18(3A): 1527–1532, 1998.

[216] **Yaman I, Balikci E.** Protective effects of Nigella sativa against gentamicin-induced nephrotoxicity in rats. Exp Toxicol Pathol 2010; 62(2): 183-190.

[217] **Yehuda S, Carasso RL.** Modulation of learning, pain thresholds, and thermoregulation in the rat by preparations of free purified alpha-linolenic and linoleic acids: determination of the optimal omega 3-to-omega 6 ratio [J]. Proc Natl Acad Sci USA, 1993, 90(21): 10345-10349.

[218] **Yildiz F , Coban S, Terzi A, Ates M, Aksoy N, Cakir H, et al.** Nigella sativa relieves the deleterious effects of ischemia reperfusion injury on liver. World J Gastroenterol 2008; 14(33): 5204-5209.

[219] **Yildiz F, Coban S, Terzi A, Savas M, Bitiren M, Celik H, et al.** Protective effects of Nigella sativa against ischemia-reperfusion injury of kidneys. Ren Fail 2010; 32(1): 126-131.

[220] **Yimer, E.M.; Tuem, K.B.; Karim, A.; Ur-Rehman, N.; Anwar, F.** Nigella sativa L. (Black Cumin): A Promising Natural Remedy for Wide Range of Illnesses. Evid. Based Complement. Alternat. Med. 2019, 2019, 1528635.

[221] **Yousefi, M., Barikbin, B., Kamalinejad, M., Abolhasani, E., Ebadi, A., Younespour, S., Manouchehrian, M., Hejazi, S., 2013.** Comparison of therapeutic effect of topical Nigella with Betamethasone and Eucerin in hand eczema. J. Eur. Acad. Dermatol. Venereol. 27, 1498-1504.

[222] **Zafeer MF, Waseem M, Chaudhary S, Parvez S.** Cadmium-induced hepatotoxicity and its abrogation by thymoquinone. J Biochem Mol Toxicol 2012; 26(5): 199-205.

[223] **Zahra Gholamnezhad, Shahrzad Havakhah, Mohammad Hossein Boskabady (2016):** Preclinical and clinical effects of Nigella Sativa and its constituent, thymoquinone: A review, Journal of Ethnopharmacology http://dx.doi.org/10.1016/j.jep.2016.06.061

[224] **Zaoui A, Cherrah Y, Aloui K, Mahassine N, Amarouch H, Hassar M (2002).** Effect of Nigella sativa fixed oil on blood homeostasis in rat. J. Ethnopharmacol. 79(1):23-26.

[225] **Zaoui A, Cherrah Y, Lacaille-Dubois M, et al.** Diuretic and hypotensive effects of Nigella sativa in the spontaneously hypertensive rat [J]. Therapie, 2000, 55(3): 379-382.

[226] **Ziaee T, Moharreri N, Hosseinzadeh H.** Review of pharmacological and toxicological effects of Nigella sativa and its active constituents. J Medicinal Plants 2012; 11:16-42.

# Computational Dynamics Study for Polymer Blend of Polystyrene, Polypropylene and Natural Rubber

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## 1. Abstract

This work introduces a sustainable Molecular Dynamics Simulation in studying the miscibility of the polymer blends, which act as a basis for analysis before laboratory experiment. The simulation software use was Material studio version 17.1, using the Forcite and Blend Modules for the computation. Temperature effect is considered on the blend mixtures as free energy of mixing (Gm), the Flory-Huggins interaction parameter (Chi or χ), the mixing energy (Emix) and the phase behaviors were analyzed during the study. The generally accepted measure of miscibility in blend mixtures is when interaction parameter (Chi or χ) is negative or less than 1 and non-miscibility when it is positive or greater than 1 is employed in this study. The results of the simulation showed that PS/PP, PS/NR and PP/NR blends were miscible at 386 K, 267 K and 175 K respectively. The miscibility points led to the evaluation of mixing energies of 0.769 kcal/mol, 0.533 kcal/mol and 0.346 kcal/mol for PS/PP, PS/NR and PP/NR blends respectively. Also, the phase behaviors of the blend mixtures were analogous and have a single critical point. The critical points correspond to an optimal mole fraction of 0.5 for the mixtures at 289 K, 202 K and 134 K for PS/PP, PS/NR and PP/NR blends respectively. The study results implied that PS will be miscible with the PP and NR at all temperatures above 386 K. The favorable interaction observed when PS is mixed with PP and NR is due to the non-polar nature of the polymers. The results achieved are in agreement with the theory.

**Keywords:** Polymer Blend, Material Studio, Polystyrene, Polypropylene, Natural Rubber.

# دراسة الديناميكيات الحسابية لمزيج البوليمر من البوليسترين والبولي بروبيلين والمطاط الطبيعي

**الملخص:** يقدم هذا العمل محاكاة ديناميكية جزيئية مستدامة في دراسة اختلاط خلائط البوليمر ، والتي تعمل كأساس للتحليل قبل التجربة المعملية. كان استخدام برنامج المحاكاة هو Material studio الإصدار 17.1 ، باستخدام Forcite و Blend Modules للحساب. تم اعتبار تأثير درجة الحرارة على خلطات المزج كطاقة حرة للخلط (Gm) ، ومعامل تفاعل Flory-Huggins (Chi أو (، وطاقة الخلط (Emix) وسلوكيات الطور تم تحليلها أثناء الدراسة. المقياس المقبول عمومًا للامتزاج في خلطات المزج هو عندما تكون معلمة التفاعل Chi) أو (χ سالبة أو أقل من 1 وعدم الامتزاج عندما تكون موجبة أو أكبر من 1 يتم استخدامها في هذه الدراسة. أظهرت نتائج المحاكاة أن خلائط / PS PPو PS / NR و PP / NR كانت قابلة للامتزاج عند 386 كلفن و 267 كلفن و 175 كلفن على التوالي. أدت نقاط الامتزاج إلى تقييم طاقات الخلط بمقدار 0.769 كيلو كالوري / مول و 0.533 كيلو كالوري / مول و 0.346 كيلو كالوري / مول لمزيج PS / PP و PS / NR و PP / NR على التوالي. أيضًا ، كانت سلوكيات الطور لخلطات المزج متشابهة ولها نقطة حرجة واحدة. تتوافق النقاط الحرجة مع جزء مول مثالي يبلغ 0.5 للمخاليط عند 289 كلفن و 202 كلفن و 134 كلفن لمزيج PS PP /و PS / NR و PP / NR على التوالي. أشارت نتائج الدراسة إلى أن PS سيكون غير قابل للامتزاج مع PP و NR في جميع درجات الحرارة فوق 386 كلفن. التفاعل الإيجابي الذي لوحظ عند خلط PS مع PP و NR يرجع إلى الطبيعة غير القطبية للبوليمرات. النتائج المحققة تتفق مع النظرية.

## 2. Introduction

It is estimated that plastic wastes produced per year represent 50% - 60% of the produced plastic goods in the same year, that is to say approximately 200 million tonnes per annum around 2020 and 10 – 20 million tonnes end up in the ocean. The plastic wastes represent an outstanding source of polymers, difficult to exploit because of practical, technical, psychological, and economic barriers (Platt, 2006; Nanda and Berruti, 2020; Mazhandu et al., 2020). However, it is also a phenomenal pollution that must be carefully treated. In any case, it is necessary to pay more for the production of a new polymer or treatment of the wastes. Which in other words, a novel material can be achieve by combining (blending) two or more of these polymers to give a unique material with improved properties (Biron, 2017).

Therefore, Polymer blends can be classified as, miscible or immiscible. Miscible blends form solutions and satisfies the thermodynamic criteria for a single-phase system which includes; PPO-PS, PVC-nitrile rubber, PBT-PET etc. while contrary, immiscible blends which is also characteristics of polymer composite and is distinguished by two or more phases that are separated by interfaces. These include toughened polymers or fibers in which elastomer are added, as the second or third phase (Charles, 2002; Zhang at al., 2003 Parameswaranpillai et al., 2014 and Mekonnen, et al., 2015). Examples of the toughed polymer are; high impact polystyrene (HIPS), modified polypropylene, acrylonitrile butadiene styrene (ABS), polyvinylchloride (PVC) etc. (MacKnight, 1989; Schmidt, 2013 Salaeh, 2014).

However, there are different simulation packages use for the determination of extend of these blends (Jawalkar et al., 2007). The most common uses of atomistic simulation tools in polymer science and engineering are the prediction of polymer miscibility (Gartner and Jayaraman, 2019). Blends of polymers are desirable since they are easier to produce than novel polymers and circumvent legislative problems. Frequently a pair (or more) of polymers with desirable properties are blended in the hope that the resultant mixture will have improved characteristics (Utracki et al., 2014).

Software's has been developed over the decade for this utilization, examples include Polylab, Material Selector etc. (Wright, 2018; Singh, 2019) but with limitations of number of polymers per batch. However, Materials Studio (MS) can also be utilized to determine the solubility parameters, cohesive energy density and Flory-Huggins interaction parameter of any number of polymers, using molecular dynamics simulation and analyze this to obtain the cohesive energy density. The Mixing Task Options panel in the material studio program allows us to set head and tail atoms in repetition units as noncontact. This means that any atoms indicated as head or tail atoms in the input structures will not be allowed to come into close proximity to any other atoms in the system. Because the non-contact atoms represent the rest of the polymer, you can utilize a monomer to mimic a polymer. (Ahmadi and Freire, 2009; de Arenaza et al., 2012; Erlebach et al., 2020; Material studio modules tutorials 2017).

Therefore, the aim of this work is to use Molecular Dynamics Simulation using Forcite and Blends of Materials Studio 2017, in the framework of the Flory-Huggins model to determine the miscibility of Polypropylene, Polystyrene and Natural rubber as a toughening agent.

## 3. METHODS

The study of the polymer blends was carried out using Material Studio 2017. The Forcite and Blends modules of the software were employed. The polymer repeat units were imported from the Materials Studio, which has a wide-range collection of predefined structures. The geometries of the repeat units were optimized using Forcite before submitting to the Blend for blend calculations.

### 3.1 Optimizing the polymer structure using the Forcite module

Forcite is a molecular mechanics unit use for optimization calculations of potential energy and geometry of arbitrary molecular and periodic systems using conventional mechanics. A geometry and energy optimization were first done for each sample using the Forcite module. Optimization was used to achieved the most stable configuration and conformation of the polymer molecules. The task was changed to 'geometry optimization'. The convergence tolerance of energy and force

were set at 1.0e-4 kcal/mol and 0.005 kcal/mol respectively for a maximum iteration of 500. 'Dreiding' forcefield is selected to represents the intra and intermolecular interactions, the charges used was 'charge using QEq' and the quality 'fine'. The convergence limit was fixed at 5.0e-4e for 50 maximum iterations. Head and tail atoms of the structures are indicated by cyan and magenta color cages around the respective atoms as shown in Figure 3.1

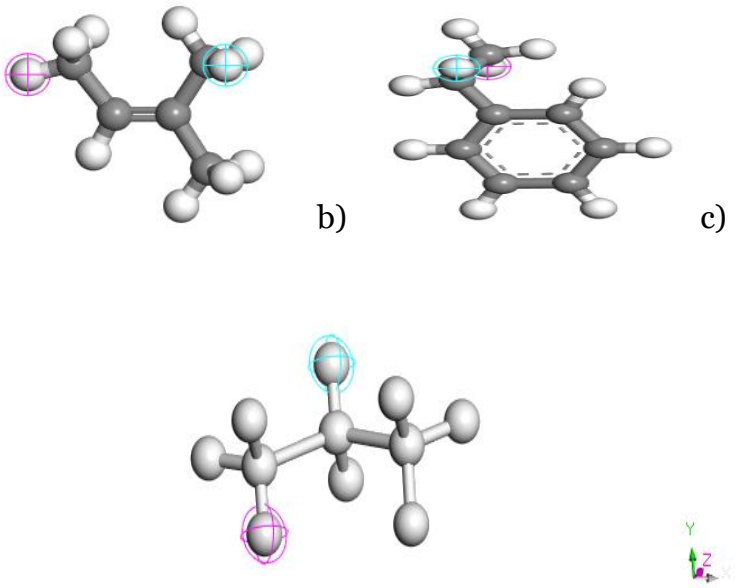


Figure 3.1: Polymer repeat unit of a) NR b) PS c) PP

### 3.2 Blending the polymers using the Blend module

The Blend module in Materials Studio has been developed to study the miscibility of polymers and solvents, significantly reducing the need for laboratory experimentation. Analysis of the result to predict miscibility, such as Flory-Huggins parameter, mixing energy and phase diagram for the blend mixtures. The module predicts the thermodynamics of polymer mixtures directly from the chemical structure of the components, therefore requires only the components molecular structures and a forcefield as an input to the blend simulation. Its exclusive superiority is the ability to combine Flory-Huggins model and molecular simulation method in calculating the compatibility of polymer mixtures (Abderaman, et al., 2018).

From the Blend module under 'Calculation', the task was changed to 'mixing' which does the binding energy and coordination number calculations, and predicts Flory-Huggins interaction parameter, mixing energy and phase behaviors. The quality was set to 'fine' and the optimized structures of PLA, PS, NR, PET, LDPE and HDPE were inserted in the input section of 'Molecule'. Blend module differentiates the components by using the property role: base or screen. Molecule with screen role is screened against one with base role. PLA was given the property role of base and PS, NR, PET, LDPE and HDPE were given the screen role.'Dreiding' forcefield was selected, the charges changed to 'charge using QEq' and the quality used was 'fine'. The convergence limit was fixed at 5.0e-4e for 50 maximum iterations.

### 3.3 Analyzing the blends using Blend module

The analysis option allowed for the study of the free energy ($G_m$), Flory-Huggins interaction parameter (Chi or $\chi$), mixing energy ($E_{mix}$) and phase behavior of the generated result.

*Analyzing the free energy ($G_m$) of the blend using Blend module:*

Combinatorial entropy contribution is the most significant factor leading to miscibility. One of the important relationships that governs this is the change of free energy of mixing ($G_m$), given by Equation 1 (Feldman, 2005; White and Wachowicz, 2008). A necessary condition for miscibility to occur is that $G_m$ must be negative ($G_m < 0$). This is a necessary requirement but not a sufficient one (Robeson, 2007). The free energy of mixing of polymers defined by the Flory-Huggins equation (equation 2) strongly depends on the value of the enthalpy of mixing or interaction contribution required for a mutual miscibility of the system. Blend module provide for the study of free energy ($G_m$) of polymer mixture (Robeson, 2007).

$$Gm = \Delta Hm - T\Delta S \qquad 1$$

$$\Delta GRT = AnAln\ A + BnBln\ B + AB \qquad 2$$

Where;

$\Delta G_m$ is the Gibbs free energy of mixing per mole, $\Delta H_m$ is the enthalpy of mixing, $\Delta S_m$ is entropy factor, T is absolute temperature, φ is the composition (volume fraction

of one of the components) $n_i$ is degree of polymerization of component i, χ is interaction parameter and R is the gas constant.

For the analysis of the free energy ($G_m$) result for each of PLA/PS, PLA/NR, PLA/LDPE, PLA/HDPE AND PLA/PET, temperature range between 298-500 K, temperature steps of 4 and mole fraction between 0-1 were specified.

*Analyzing the interaction parameter (Chi or χ) of the blend mixtures using Blend module:*

Flory-Huggins interaction parameter is the central measure in the Flory-Huggins theory. According to the Flory-Huggins theory, for two molecules have better miscibility and a favorable interaction at a particular temperature a negative value or a value less than 1 of interaction parameter is required (Robeson, 2007; Abderaman, et al., 2018). It is likely of the two components to show just one phase at this temperature. If interaction parameter is positive or greater than 1, the molecules cannot be mixed, but rather prefer to be surrounded by similar components than each other. The interaction parameter is used to indicate miscibility of polymer blends and the miscibility points (temperature). Blend module allows for this analysis.

For this analysis, temperature range between 298-500 K and 25 steps were specified for each of the PLA/PS, PLA/NR, PLA/LDPE, PLA/HDPE and PLA/PET blend the

*Analyzing the mixing energy ($E_{mix}$) of the blend mixtures using the Blend module:*

Generally, it is admitted that a value of the mixing energy ($E_{mix}$) close to zero indicates miscibility (Abderaman, et al., 2018). The more $E_{mix}$ increases, the less the miscibility. The relationship between Flory-Huggins interaction parameter and mixing energy is given by Equation 3.

$$\chi = \text{EmixRT} \qquad 3$$

Blend module was also used to analyze the mixing energy ($E_{mix}$) of the blend results. The temperature range between 298-500 K and 25 steps were specified for the blend mixtures.

*Analyzing the phase behavior of the blend mixtures using Blend module:*

Phase diagram in polymer blend is employed to check critical point, which marks the start of coexistence region. The coexistence region is linked by the binodal, indicated by blue lines. While the spinodal, indicated by green lines separates the coexistence region into two regions. In the region between the binodal and the spinodal the mixture is metastable, where the mixture will begin to separate only after a sufficiently large fluctuation. But in the spinodal region the mixture is unstable; any fluctuation will cause the spontaneous separation of the mixture. Similarly, the maximum of the spinodal corresponds to the critical point. In other words, above the binodal region the mixture is stable. Blend module is used for this analysis (Robeson, 2007; Young, 2014).

For the study of the phase behavior of the blend result of each of the blend of PLA with PS, NR, LDPE, HDPE and PET, 25 steps were specified.

## 4. Results

The blends were carried out at 298 K and the results are presented below. The analysis of the free energy ($G_m$), interaction parameter ($\chi$), mixing energy ($E_{mix}$) and phase behavior of the blends are carried out in order to examine the miscibility between the polymers.

### 4.1 Free energy of mixing ($G_m$)

The free energy of mixing ($G_m$) results generated for the blend of PP, PS and NR between the temperature range of 298-500 K, temperature steps of 4 and mole fraction between 0-1 are shown in Figure 3.1-3.3.

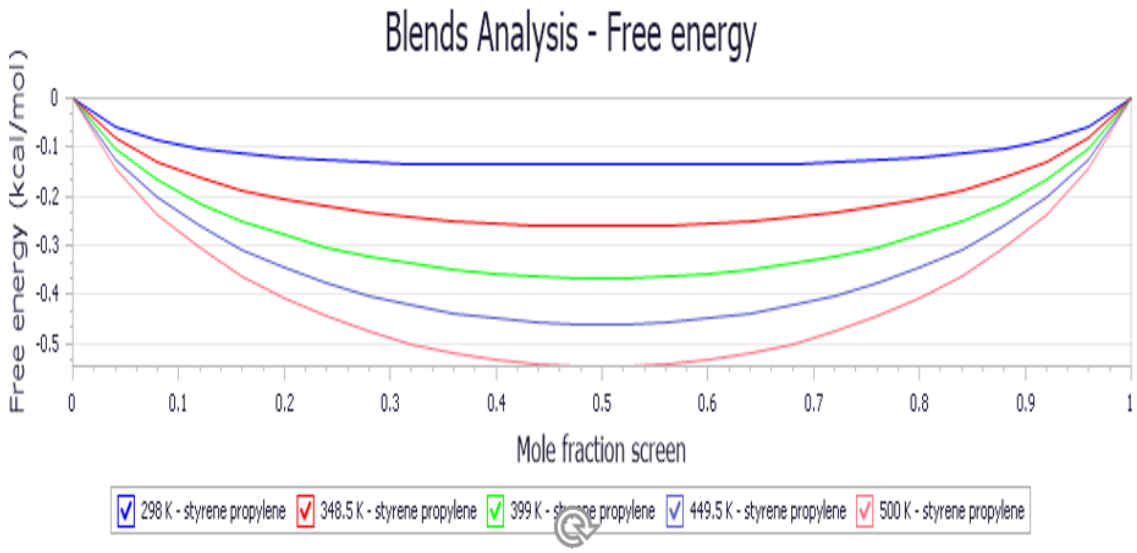


Figure 4.1: Free energy analysis for binary system of PS/PP.

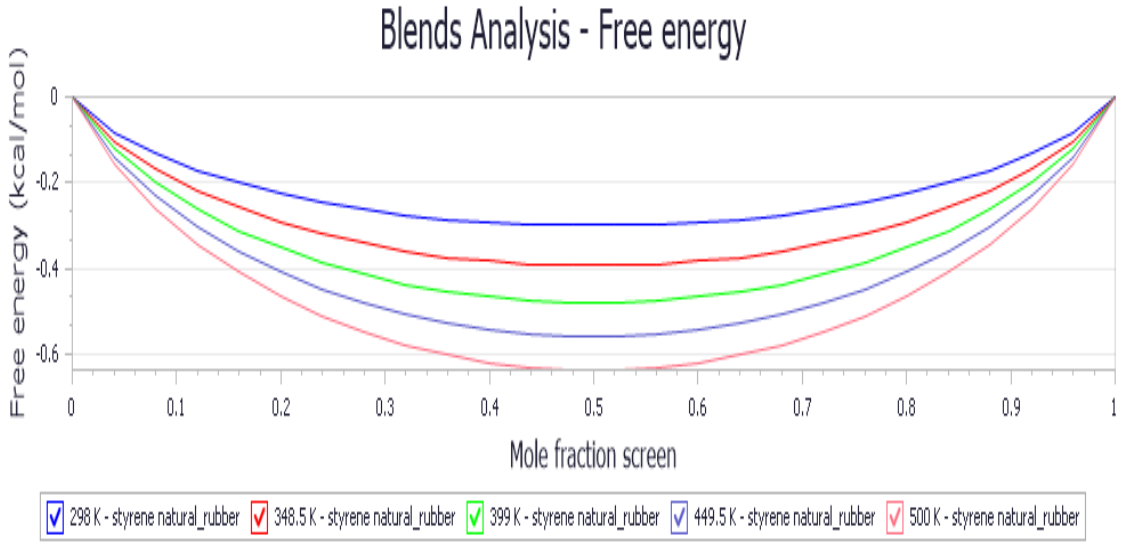


Figure 4.2: Free energy analysis for binary system of PS/NR.

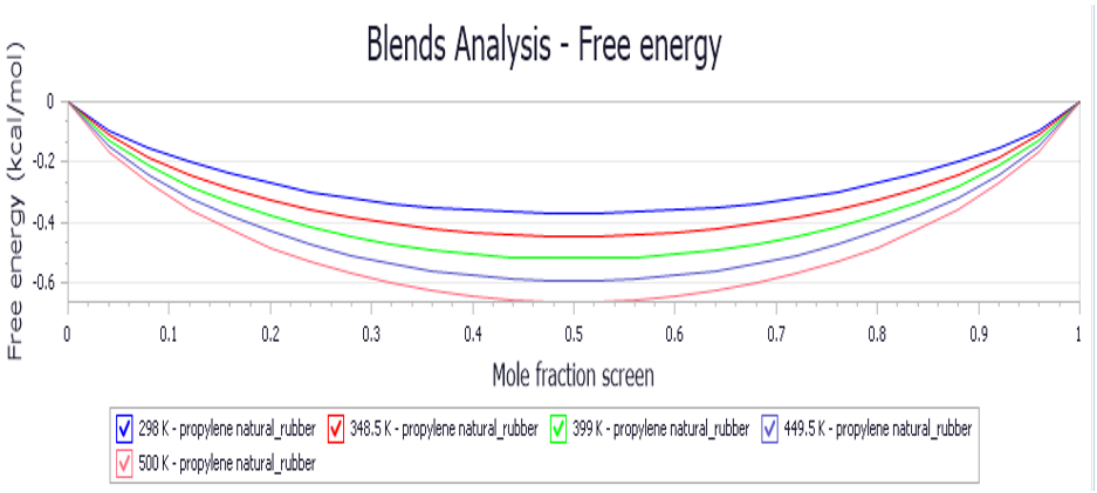


Figure 4.3: Free energy analysis for binary system of PP/NR.

The free energy ($G_m$) of mixing for the blend of PP, PS and NR in Figure 4.1-4.3 shows that the energy values are all less than zero and the values further decrease as temperature is increase. This result is in line with literature that a necessary condition for miscibility to occur is that $G_m$ must be negative ($G_m < 0$) (Robeson, 2007). This result agreed with the theory of Equation 1, relationship between free energy and temperature.

## 4.2 Flory-Huggins interaction parameter (χ or Chi)

From Figure 4.4, the interaction parameter (χ or Chi) is plotted as a function of the temperature for mixture of PP, PS and NR. This shows the dependence of interaction parameter (χ or Chi) on temperature.

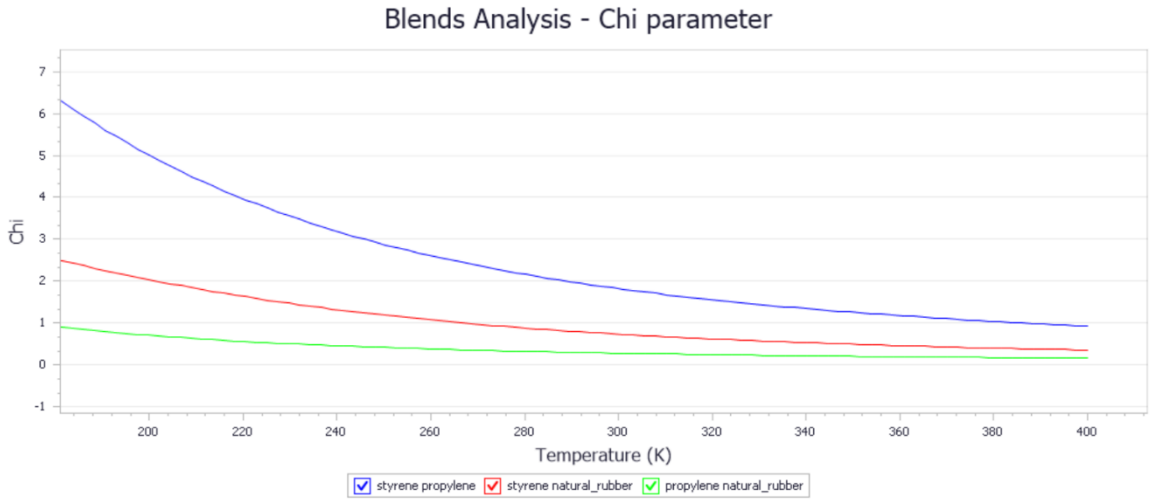


Figure 4.4: Interaction parameter (χ or Chi) analysis.

Miscibility point for PS/PP, PS/NR and PP/NR are found at 386 K, 267 K and 175 K respectively.

According to the Flory-Huggins theory, a negative value or a value less than 1 of Chi (χ) indicates that at this particular temperature the two molecules have better miscibility and a favorable interaction (Abderaman, et al., 2018). If χ is greater than one the molecules cannot be mixed, rather prefer to be surrounded by similar components. From Figure 4.4, it is observed that the Chi (χ) parameter values of blends decrease as the temperature increase. This implies that for a miscible system, increase in temperature decrease Chi (χ) parameter which is measure of increasing miscibility. The result shows that PP/NR had the best miscibility at the lowest temperature of 175 K, followed by PS/NR at 267 K and PS/PP at 386 K accordingly Thus, the results reinforce that of the free energy ($G_m$), that PP, PS and NR will be miscible.

### 4.3 The mixing energy ($E_{mix}$)

Figure 4.5 $E_{mix}$ is plotted as a function of the temperature, for mixture of PP, PS and NR.

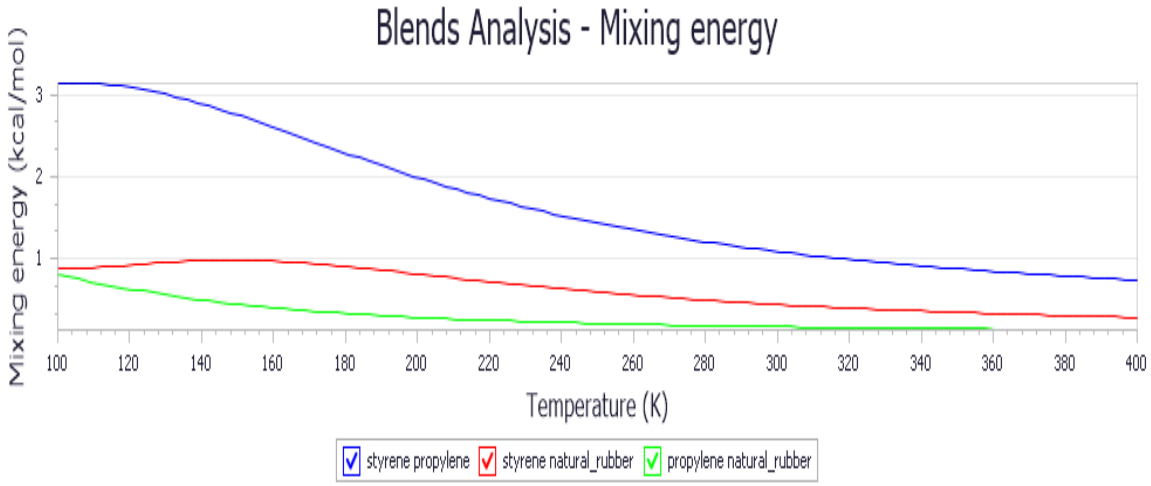


Figure 4.5: Mixing energy ($E_{mix}$) analysis

The result in Figure 3.5 led to the evaluation of a mixing energy of 0.769 kcal/mol at 386 K for PS/PP, 0.533 kcal/mol at 267 K for PS/NR and 0.346 kcal/mol at 175 K for PP/NR.

A mixing energy ($E_{mix}$) of a blend mixture close to zero also indicates miscibility (Abderaman, et al., 2018). The more $E_{mix}$ decreases, the more the miscibility. The

analysis of the graph in Figure 4.5 shows that when the temperature increases, the $E_{mix}$ of the blends decreases. This justified the linear relationship between Chi ($\chi$) parameter and mixing energy ($E_{mix}$) in Equation 2. At the achieved miscibility points of the blends, mixing energy of 0.769 kcal/mol, 0.533 kcal/mol and 0.346 kcal/mol for PS/PP, PS/NR and PP/NR respectively. The mixing energy ($E_{mix}$) result reinforce that of the interaction parameter ($\chi$), that PP/NR had the best miscibility, followed by PS/NR and PS/PP.

### 4.4 The phase behavior of the binary mixtures

The phase diagrams of the blends of PP, PS and NR are shown in Figure 3.6-3.8, where the composition of the mixture is given as a function of the mole fraction screen of the other polymers. The phase diagram generally contains three pieces of information: critical points (red), spinodal (green) and binodal (blue). In phase diagrams, a critical point marks the start of coexistence region. However, the mixture is unstable in the spinodal region. Metastable in the region between the spinodal and binodal. But, stable in the binodal region.

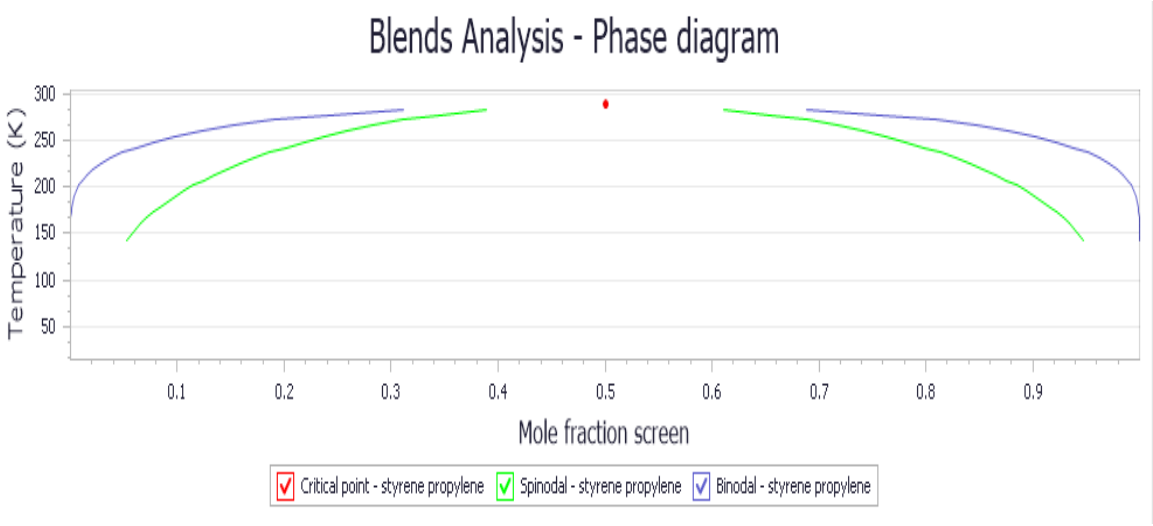


Figure 4.6: Phase diagram for binary system compound of PS/PP.

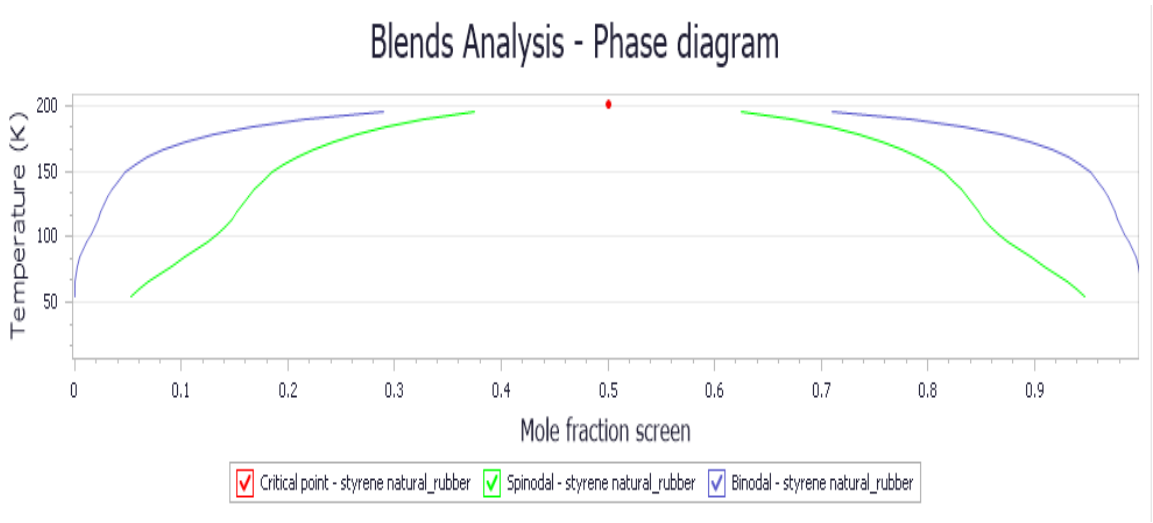


Figure 4.7: Phase diagram for binary system compound of PS/NR.

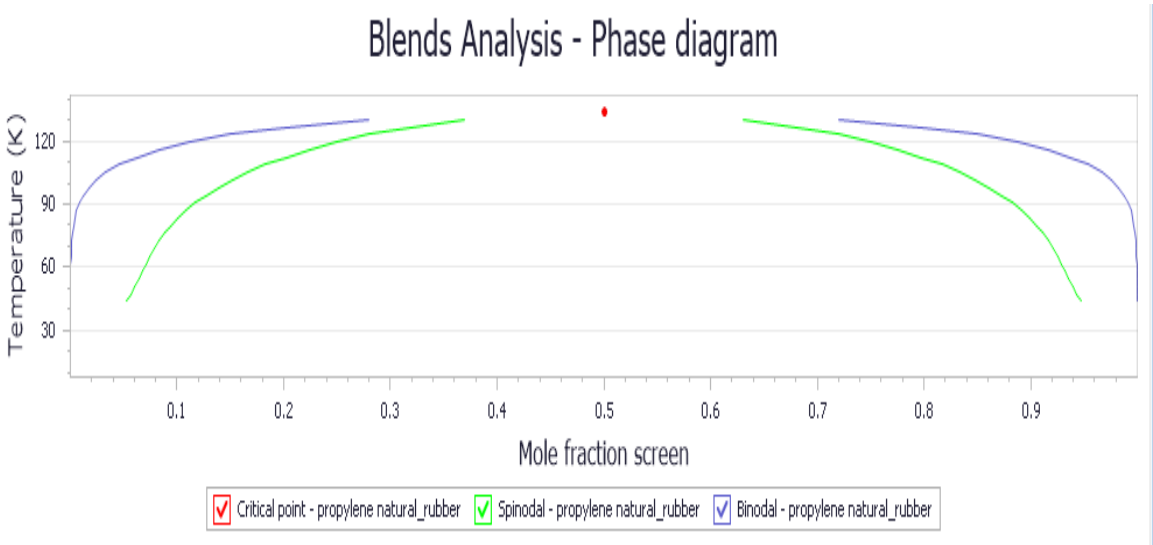


Figure 4.8: Phase diagram for binary system compound of PP/NR.

The results have shown that the critical point temperatures of PS/PP, PS/NR and PP/NR are 289 K, 202 K and 134 K respectively, at an optimum mole fraction of 0.5 for all the systems. Analyzing the phase behavior, it is observed that the blends of PP, PS and NR all have a simple critical point and one coexistence region.

## 5. CONCLUSION

The study of the miscibility between the blend mixtures of PP, PS and NR by molecular dynamics simulation was carried out using Material Studio 17. The free energy, Flory-Huggins interaction parameter, mixing energy and phase diagrams of blend mixtures were analyzed. Miscibility points for PS/PP, PS/NR and PP/NR

blends were found at 386 K, 267 K and 175 K respectively. The auspicious interaction observed when PS is mixed with PP and NR is due to the non-polar nature of the polymers. The results led to the evaluation of a mixing energy of 0.769 kcal/mol, 0.533 kcal/mol and 0.346 kcal/mol for PS/PP, PS/NR and PP/NR blends respectively. Likewise, the mixtures of PS, PP and NR all have a simple critical point and one coexistence region. The critical points of PS/PP, PS/NR and PP/NR blends are found at 289 K, 202 K and 134 K respectively, at an optimal mole fraction of 0.5 for all the mixtures. Then, it can be said that for a mole fraction of 0.5 and a temperature of 386 K, PS is miscible with all the other polymers (PS or NR).

## REFERENCE

[1] Abderaman, M. B., Gueye, E. H. O., Dione, A. N., Diouf, A. A., Faye, O., & Beye, A. C. (2018). A Molecular Dynamics Study on the Miscibility of Polyglycolide with Different Polymers. International Journal of Materials Science and Applications, 7(4), 126.

[2] Ahmadi, A., & Freire, J. J. (2009). Molecular dynamics simulation of miscibility in several polymer blends. *Polymer*, *50*(20), 4973-4978.

[3] Biron, M. (2017). Recycling: The First Source of Renewable Plastic. *Industrial Applications of Renewable Plastics*, 67-114. **http://dx.doi.org/10.1016/B978-0-323-48065-9.00003-0**

[4] Charles, H. (2002). Handbook of Plastics, Elastomers and Composites. McGraw-Hill Professional, USA. p. 69 ISBN 0-07-138476-6

[5] de Arenaza, I. M., Meaurio, E., & Sarasua, J. R. (2012). Analysis of the miscibility of polymer blends through molecular dynamics simulations. *Edited by Ailton De Souza Gomes*, 29.

[6] Erlebach, A., Muljajew, I., Chi, M., Bückmann, C., Weber, C., Schubert, U. S., & Sierka, M. (2020). Predicting Solubility of Small Molecules in Macromolecular Compounds for Nanomedicine Application from Atomistic Simulations. *Advanced Theory and Simulations*, *3*(5), 2000001.

[7] Feldman, D. (2005). Polyblend compatibilization. *Journal of Macromolecular Science, Part A: Pure and Applied Chemistry*, *42*(5), 587-605.

[8] Gartner III, T. E., & Jayaraman, A. (2019). Modeling and simulations of polymers: a roadmap. *Macromolecules*, *52*(3), 755-786.

[9] Jawalkar, S. S., Raju, K. V., Halligudi, S. B., Sairam, M., & Aminabhavi, T. M. (2007). Molecular modeling simulations to predict compatibility of poly (vinyl alcohol) and chitosan blends: a comparison with experiments. *The Journal of Physical Chemistry B*, *111*(10), 2431-2439.

[10] MacKNiGHT, W. J. (1989). Polymer Blends WiLLiAM J. MacKNiGHT and FRANK E. KARASZ University of Massachusetts, Amherst, MA, USA. *Comprehensive Polymer Science: Specialty polymers and polymer processing*, *7*, 111.

[11] Mazhandu, Z. S., Muzenda, E., Mamvura, T. A., & Belaid, M. (2020). Integrated and Consolidated Review of Plastic Waste Management and Bio-Based Biodegradable Plastics: Challenges and Opportunities. *Sustainability*, *12*(20), 8360.

[12] Mekonnen, T. H., Misra, M., and Mohanty, A. K. (2015). Processing, performance, and applications of plant and animal protein-based blends and their biocomposites. In *Biocomposites* (pp. 201-235).

[13] Nanda, S., & Berruti, F. (2020). Thermochemical conversion of plastic waste to fuels: a review. *Environmental Chemistry Letters*, 1-26.

[14] Parameswaranpillai, J., Thomas, S., and Grohens, Y. (2014). Polymer blends: state of the art, new challenges, and opportunities. *Characterization of polymer blends: miscibility, morphology and interfaces*, 1-6.

[15] Platt, D. K. (2006). *Biodegradable polymers: market report*. iSmithers Rapra Publishing.

[16] Robeson, L. M. (2007). Polymer blends. *A Comprehensive Review*. First Edition. Munich, Germany: Hanser Publishers, ISBN-10: 3-446-22569-2, ISBN-13: 978-3-446-22569-5

[17] Salaeh, S. (2014). *Processing of natural rubber composites and blends: relation between structure and properties* (Doctoral dissertation, Université Claude Bernard-Lyon I).

[18] Schmidt, A. (2013). *Handbook of Polymer Synthesis, Characterization and Processing*. *Edited by Enrique Saldívar-Guerra and Eduardo Vivaldo-Lima*. *Angewandte Chemie International Edition, 53(2), 358–358*. doi:10.1002/anie.201309282

[19] Singh, A., Radhakrishnan, S., Vijayalakshmi, R., Talawar, M. B., Kumar, A., & Kumar, D. (2019). Screening of polymer-plasticizer systems for propellant binder applications: an experimental and simulation approach. *Journal of Energetic Materials*, *37*(4), 365-377.

[20] Utracki L.A., Mukhopadhyay P., Gupta R.K. (2014) Polymer Blends: Introduction. In: Utracki L., Wilkie C. (eds) Polymer Blends Handbook. Springer, Dordrecht. https://doi.org/10.1007/978-94-007-6064-6_3

[21] White, J. L., & Wachowicz, M. (2008). Polymer blend miscibility. *Annual Reports on NMR Spectroscopy*, *64*, 189-209.

[22] Wright, C. J. (2018) Case Study: Practical Introduction of a Materials Selection Software in a Fundamentals of Materials Science Course.

[23] Young, N. P. (2014). *Thermodynamics and phase behavior of miscible polymer blends in the presence of supercritical carbon dioxide* (Doctoral dissertation, UC Berkeley).

[24] Zhang, G., Zhang, J., Wang, S., & Shen, D. (2003). Miscibility and phase structure of binary blends of polylactide and poly (methyl methacrylate). *Journal of polymer science part B: Polymer physics*, *41*(1), 23-30.

# هيئة التحرير

# الهيئة الاستشارية

# قواعد النشر في المجلة

- أن يكون البحث جديدا، ولم يسبق نشره
- أن يتسم بالأصالة والجدة والابتكار والاضافة للمعرفة
- أن لا يكون مستلا من بحوث سبق نشرها للباحث/للباحثين
- أن تراعى فيه قواعد البحث العلمي الاصيل، ومنهجيته.
- أن يشتمل البحث على:
  - ✓ صفحة عنوان البحث باللغة الانجليزية.
  - ✓ مستخلص البحث باللغة الانجليزية.
  - ✓ صفحة عنوان البحث باللغة الانجليزية.
  - ✓ مستخلص البحث باللغة العربية.
  - ✓ مقدمة.
  - ✓ صلب البحث.
  - ✓ خاتمة تتضمن نتائج وتوصيات.
  - ✓ ثبت المصادر والمراجع.
  - ✓ الملاحق الملازمة( إن وجدت.)
- في حال (نشر البحث ورقا )يمنح الباحث نفسه نسخة من عدد المجلة الذي نشر بحثه بها و10 نسخ من بحثة بشكل مستقل
- في حال اعتماد نشر البحث تؤول حقوق نشره كافة للمجلة، ولها ان تعيد نشره ورقيا أو إلكترونيا، ويحق لها
- إدراجه في قواعد البيانات المحلية والعالمية- بمقابل أو بدون مقابل -وذلك دون حاجة للإذن الباحث.
- لا يحق للباحث إعادة نشر بحثه المقبول للنشر في المجلة- في أي وعاء من أوعية النشر -إلا بعد إذن
- كتابي من رئيس هيئة تحرير المجلة
- نمك التوثيق المعتمد في المجلة هو نمط IEEE

# معلومات الإيداع

**النسخة الورقية :**

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الرقم التسلسلي الدولي للدوريات **(ردمد)** 7936 – 1658

**النسخة الإلكترونية:**

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**الموقع الإلكتروني للمجلة:**

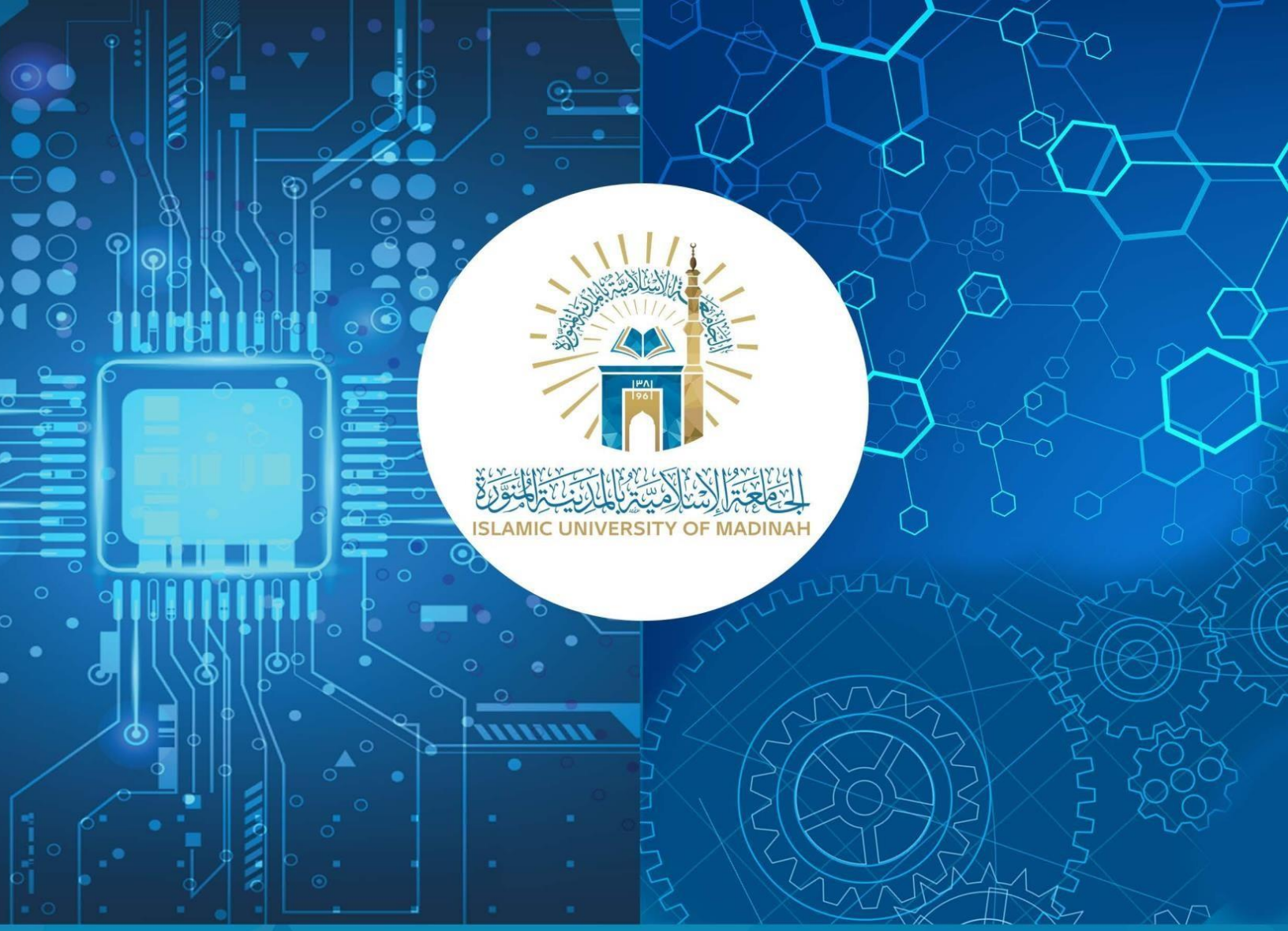
https://jesc.iu.edu.sa

**ترسل البحوث باسم رئيس تحرير المجلة إلى البريد الإلكتروني**

jesc@iu.edu.sa

**الآراء الواردة في البحوث المنشورة تعرب عن وجهة نظر الباحث فقط، ولا تعرب بالضرورة عن المجلة.**


بسم الله الرحمن الرحيم




# مجلة الجامعة الإسلامية

## للعلوم التطبيقية

مجلة علمية دورية محكمة

العدد: ١ السنة: الرابعة ١٤٤٣هـ