Exploring the Power of Nigella Sativa Seeds: A Modern Perspective on an Ancient Remedy

Abstract

Nigella sativa (N. Sativa) seeds are widely recognized for their medicinal properties, which make them valuable for both the culinary and pharmaceutical industries. The traditional plant that is most widely used is N. sativa and also known by other names like black cumin and kalonji. The N. Sativa is grown and distributed throughout India, primarily in the states of Punjab, Himachal Pradesh, Bihar, Bengal, and Assam, as well as in Bangladesh, Bangladesh, Syria, Lebanon, Israel, and South Europe. Numerous beneficial and bioactive chemical components, including thymoquinoline, thymoquinone, alpha hydrine, alpha pinene, p-cymene, alkaloides like nigellicimine and nigellicimine N-oxide,sesquiterpenes and thymol, are found in N. Sativa. Due to these bioactive chemical constituents N. Sativa have many biological activities like antimicrobial, anti-inflammatory, antioxidant, antibiotic etc. The review helps to introduce about the current trends about N. Sativa, including phytochemical screening, methods of extraction, methods of isolation of chemical constituents of N. Sativa, therapeutic and biological activity of N. Sativa, computational approaches which helps in find the relationship of phytoconstituents of N. Sativa seeds with receptor. Some new trends which help in enhance the activity on N. Sativa.

Keywords: *Nigella Saiva seeds, methods of extraction, computational approaches, chemical constituents, pharmaceutical activities.*

1. Introduction

People in the twenty-first century are drug dependent due to a wide range of illnesses and lifestyle choices. Worldwide, homeopathy, Ayurveda, and allopathy are among the most well- liked medical specialties. The main sources of bioactive molecules, which have frequently been used to treat diseases, are natural products, secondary metabolites, and bioactive molecules produced from plants, animals, and microbes [24]. They contend that people depend on these medical professionals. Medicine is the science of healing, encompassing the prevention and treatment of disease as well as the practice of diagnosis and health promotion. It also discusses pharmaceuticals, plant-based substances, and medications used to improve and treat a variety of illnesses. "The art of illness prevention" is how the dictionary describes medicine. [1] Since ancient times, drugs derived from plants have been used to cure or lessen medical conditions in people. Native American medicine is becoming more and more popular over time, primarily due to the fact that herbal remedies have few or no harmful side effects. Researchers' interest in the conventional treatments utilized by prehistoric tribes and ancient

civilizations has grown at the same time. It is thought that studying these old medications with contemporary scientific tools and techniques could reveal a plethora of efficient treatments for curing illnesses and easing human suffering. An estimated 2,500 000 to 5,000 000 plant species are used to cure a wide range of illnesses and are believed to have therapeutic qualities.

Fig 1. N. Sativa Plant [25]

Fig 2. Seeds of N. Sativa

Throughout most of Asia, the use of traditional medicinal herbs for health purposes is encouraged by a culture that has been passed down through the years. In ancient India, Egypt, and China, the list of therapeutic plants, their availability, and their applications dates back to at least 3,500 BC. [2]. Indians are among the oldest civilizations to have demonstrated the efficacious use of food products in medicine and treating illnesses; Ayurveda has been supporting this idea for five millennia [23]. India has been acknowledged from the ancient times for spices. Spices have been recognized as culinary and powerful medicinal ingredient form the ancient times in India. Spices' ability to impart biological activity is becoming more and more of a topic of research for human health. A substantial portion of agricultural commodities and a vital part of our country's economy are the seed spices. India grows roughly twenty different types of spice seed. The most common ones are nigella, celery, anise, caraway, fennel, fenugreek, cumin, coriander, and ajwain. Many phytochemicals, or secondary metabolites, are produced by seed spices. For thousands of years, people have utilized Nigella sativa (N. sativa) seeds are obtained from the *Nigella sativa Linn.* Belonging from the family Ranunculaceae, often also known as 'black seeds' and used as a spice, food preservative, and protective and curative treatment for verity of disease

1.1. Taxonomic classification:

N. sativa taxonomically classified from the kingdom of plantae, subkingdom of tracheobionta, superdivision spermatophyte, phylum magnoliophyta, class Magnoliopsida, order Ranunculales, family Ranunculaceae, genus nigella and species sativa.

1.2.Common names

N. Sativa is also named from the different name in different countries as black cumin, black seed, habba Saouda, black caraway, Roman coriander, Damascena, Devil in the Bush, and senoudj or sinoudj [4-5].

1.3.Geographical Distribution of Nigella sativa

The plant is cultivated in Southern Europe, Bangladesh, Turkey, the Middle East, Israel, Lebanon, Syria, and the Mediterranean basin, as well as in India. Cool, dryto warm, humid climates are ideal for the species' growth. Weather that is cool and humid encourages seed set and blossoming. The species is grown once a year in the rabi season (April to end of May in hills, October to November in plains) in any good soil. The yield per acre is not good. It has been reported that the yield of black cumin seeds is 8.13 q/ha [16]. The seeds can be purchased in the Indian market. The species is reportedly very good for small-scale farmers to cultivate. Native to countries bordering the Mediterranean Sea, such as Egypt, Turkey, and Italy, is the herbaceous plant Nigella sativa. We don't know exactly who it is. Known by another name, Nigella indica, Roxburgh believes that this plant originated in India. It is extensively cultivated, especially in India, Pakistan, Iran, Syria, Turkey, Ethiopia, Oman, and Saudi Arabia, for a wide range of industrial and pharmaceutical purposes (food and therapeutic uses). It grows naturally in Southwest Asia, the Middle East, southern Europe, and North Africa. [2,5]

1.4.Morphological characters of N. Sativa:

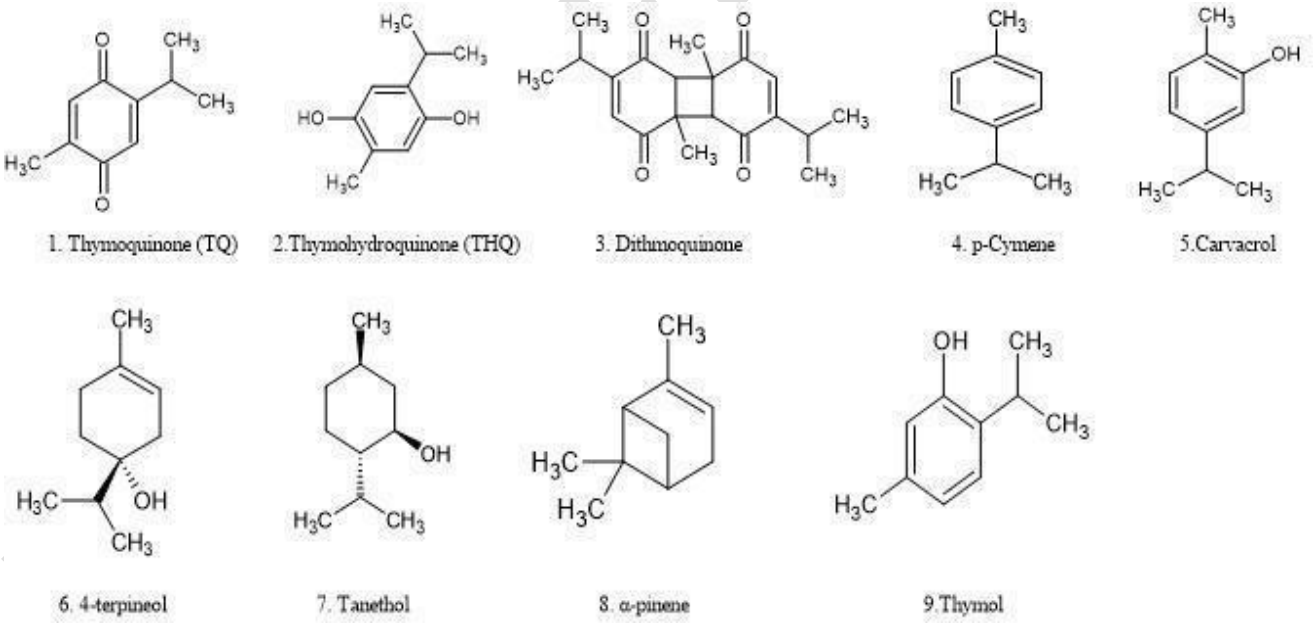
N. sativa is a flowering annual that reaches heights of 20 to 90 cm. It has finely split leaves. It blooms in white, yellow, pink, pale blue, or pale purple with five to ten petals. The fruit is a large, inflated capsule composed of three to seven follicles that are attached to one another and contain several seeds. Small, trigonous, tubercular, angular, dicotyledonous seeds with a bitter flavor and a hint of aromatic aroma. Their exterior is black, and their interior is white. [3,6].

2.CHEMICAL CONSTITUENTS

The plant consists of about 171 chemical components, many of which have multiple biological activities, make up the plant. These constituents include lipids, proteins, carbohydrates, crude fibers, vitamins, resins, reducing sugars, and esters of unsaturated fatty acids [7]. The most significant active constituents are p-cymene, carvacrol, 4-terpineol, tanethol, sesquiterpene longifolene, thymoquinone, and carvacrol. Among the key active components are carvacrol, 4-terpineol, tanethol, sesquiterpene longifolene, alpha-pinene, and nigellicine. The water-soluble pentacyclic triterpenes alpha-hederin andsaponin, which are thought to have anticancer properties.

Linoleic acid, oleic acid, eicosadienoic acid, and dihomolinoleic acid are the main unsaturated fatty acids found in N. sativa seeds. Less than 30% of the seeds' remaining content is made up of saturated fatty acids, such as palmitic and stearic acid. In addition to vitamins and minerals like copper, phosphorus, zinc, and iron, the seeds also include protein (26.7%), fat (28.5%), carbs (24.9%), crude fiber (8.4%), and total ash (4.8%). Sitosterol is an important sterol that makes up 44% to 54% of the total sterols in Tunisian stigmasterol, which has a range of 6.57% to 20.92%. Other ingredients include butyrospermol, cycloartenol, 24-methylene-cycloartanol, taraxerol, citrostadienol, lophenol, obtusifoliol, nigellone, campesterol, cholesterol, stigmasterol-7-ene, and tirucallol; oleic acid; esters of unsaturated fatty acids with C15 and higher terpenoids; aliphatic alcohol; melanthin, melanthigenin, bitter principle; tannin, resin, protein, reducing sugar, glycosidal saponin, hederagenin, volatile oil (0.5-1.6%), fatty oil (35.6-41.6%), etc.

Fig. 3. Few Bioactive Chemical Constituents present in N. Sativa



3. Method of Extraction

To extract bioactive components from N. sativa seeds, a variety of techniques can be used. A few extraction techniques are explained here:

3.1. Maceration: The maceration process can be used to prepare N. sativa seed extracts. After giving the seeds, a thorough cleaning with distilled water, let them air dry for three days at room temperature in the shade. The goal of shadow drying is to guarantee their cleanliness and get rid of any potential impurities. The seeds were roughly 10g in

powder, steeped in distilled water (1:10), and let tostand at room temperature for 24 hours while being constantly stirred at 150 rpm. The yellowish extract was then filtered using Whatman No. 42 filter paper and kept for lateruse at 4 ◦C. [10]

3.2. Percolation Extraction: Put 1 g of black seed and 20 mL each of hexane and methanol into two different conical flasks. For four hours, the mixture is heated on a water bath at 40°C. After centrifuging the extract solution for 10 minutes at 4000 rpm and 4°C, filter the mixture. [11]

3.3. Noval techniques for extraction of from N. Sativa seeds

3.3.1. Cold Pressing Extraction Method

There are numerous techniques for obtaining oil from Nigella sativa seeds. Nigella sativa oil can be extracted from seeds using the cold pressing technique, according to Kiralan et al. The process involved using a mechanical press to apply pressure to seeds at a temperature of 25 °C. In order to aid in the separation of the oil from the crushed seed fiber, the solution was also submerged for one night at a temperature of 25 °C and then filtered.

3.3.2. Supercritical Fluid Extraction

Mohammed et al. employed yet another creative technique to extract oil from seeds of N sativa. Using a stainless-steel grinder for three to four minutes, the supercritical fluid extraction apparatus was utilized to extract the oil from the Nigella sativa seed. The material was then transferred into a 50-liter extractor container and securely sealed. To maintain the temperature at 40 °C for an hour, the system used an automated back pressure regulator. And injection rate of liquid carbon dioxide (CO_2) was 150 L/h, and the pressure was 600 bar.

The supercritical fluid extraction method was also selected by Rao et al. to extract the oil from the seeds of N. sativa. A 260 mL syringe pump, an ISCO 260D controller system, and an ISCO series 2000 SCF extraction system (SFX 220), which consists of two 10 mL stainless steel vessels housed within a dual chamber extraction module, made up the instrumentation. As a result, 10 mL of stainless-steel cell was filled with about 5 g of powdered seeds. After that, the cell was filled to a standard volume of 50–400 mL with 1 mL/min of supercritical carbon dioxide (SC CO2). In the cold trap, the extract's final concentration was gathered. The yield at 508°C, 400 bar, and 100 mL was found to be 0.84% after the supercritical fluid extraction conditions were optimized.

3.3.3. Soxhlet Extraction

Using Soxhlet apparatus, Dinagaran et al. extracted oil from seeds of N. sativa. To achieve this goal, seeds were gathered from various locations of India. The tiny, infected seeds were taken out and allowed to sit at room temperature for the sorting process. After roughly two hours, the seeds were ground using a tabletop combination, and the oil was extracted using hexane via the Soxhlet system. The extracted oil was then stored by using an amber colour glass jar at room temperature until needed. The most of the constituent found was 28–35% fixed oil which consists of saturated fats. An analysis conducted through gas chromatography-mass spectrometry (GC-MS) revealed that black seeds comprised 32 distinct types of compounds.

3.3.4. Hydro Distillation (HD) Extraction Method

Kokoska et al. used the hydro distillation (HD) process to extraction of oil from N. sativa seeds. Initially, the N. Sativa

seeds were ground at a 25 °C temp. Subsequently 70g of sample used for further analysis. Dry weight computation was used to compute the yields and average them. In order toextract essential oil using the HD method, the material was placed within a water-resistant flask. This setup is referred to as a Clevenger-type device due to the direct connection between the flask and the condenser. After two continuous hours of processing, a pale-yellow oil with a weight percent of 0.29 was acquired. Burits et al. Also used the HD Methode for oil isolation, they also used the same standard apparatus—the Austrian pharmacopoeia, or Clevenger apparatus—for all of their experiments. The results were disappointing because just 3% of essential oil has obtained from the extracted oil. As comparison, a 48% thymoquinone concentration was obtained by the Soxhlet extraction process.

3.4. Microwave-Assisted Extraction Method (MAE)

Abedi and colleagues utilised a home microwave oven operating at 2450 MHz to extract oil. After measuring out 50 g of crushed seeds, they added 50 mL of water to a 500 mL flask and let it sit for 30 minutes. The Clevenger equipment was put together and given a 30-minute heat treatment at 450 W. The essential oil was extracted using n-hexane, giving 0.33% under the given extraction parameters.

3.5. Ultrasound-Assisted Extraction Method

Moghimi et al. extracted oil with the help of ultrasonic assistance. A 500 g sample was transferred into a 1.5 L container and subjected to ultrasonic treatment in a bath. Various optimization parameters were explored, such as treatment durations of 30, 45, and 60 minutes, and power levels of 30, 60, and 90 watts. The ultrasonic pretreatment was conducted at a steady frequency of 25 kHz. The screw press operatingat around 33 rpm was utilised to isolate the oil, following this procedure. At a power of 90 W and a duration of 60 minutes, the highest extraction efficiency achieved was 39.93%. In contrast, at a power of 30 W and a duration of 30 minutes, the lowest extraction efficiency recorded was 27.29%.

3.6. Extraction by Steam Distillation

Steam distillation was carried out at low temperature to reduce deterioration. After combining ten grams of seeds with100ml of distilled water, the blend was moved onto a separatory funnel. Three times the extraction was performed, 10ml of diethyl ether were added, and each time there was a vigorous shaking period. Sodium sulfate was used to dry the organic layer, and after evaporating in a water bath, 0.4% was obtained. Using a glass column positioned between the condenser and flask, Kokoska et al. used steam distillation. The yield of pale-yellow oil obtained by their approach was 0.39%.

3.7. Accelerated Solvent Extraction Method (ASE)

1gm of powdered black seed was added to a 34ml stainless steel cell. Pressure of 100 atm, static time of 10 minutes, 20% rinse volume, 2 extraction cycles, 30 second purge time, and 26ml solvent volume were the conditions set for the extraction. P1–P9 black seed samples were treated at 40 °C with n- hexane for P1–P3, methanol (MeOH), and dichloromethane (DCM) from Saudi Arabia, Pakistan, and India. At 50 °C, samples P4-P6 were extracted using MeOH, DCM, and n-hexane; samples P7-P9 were extracted using the same method at 70 °C. The findings showed that MeOH had the second- highest yield, following n-hexane, with 2.5 g (12.5%) for the Saudi Arabian sample and 2.2 g for the other samples. [12].

4. Phytochemical screening of N. Sativa

Phytochemical screening of the N. Sativa seed extract can be done by using hyphenated techniques, like HPLC, HPLC-MS, LC MS, GC-MS etc. but here id some laboratory based chemical testes which can be used for phytochemical

screening of many types of chemical constituents.

4.1. Total phenolic (TP) content:

The Folin-Ciocalteau method modified can be used to measure the TP: 100µl of the sample extract plus 500 µl of a 0.1 diluted solution in Milli-Q water Phenol reagent Folin-Ciocalteau Let it reactat room temperature for five minutes in the dark. Next, add 400 µl of 7.5% sodium bicarbonate, and then incubate at 30 °C in the dark for 90 minutes at 765 nm, measure the absorbance. Using the gallic acid calibration curve (R2 = 0.984), TP can be represented as mg mg GAE/g dw, or gallic acid equivalent per gram of dry matter.

4.2. Total flavonoid (TFd) content

The TFd content can be determined using a standard spectrophotometric method. Mix 0.5 ml of theextract with 0.5 ml of a 2% AlCl3 solution prepared in methanol. After 30 minutes, measure the absorbance at 430 nm against a blank for comparison.

4.3. Total flavonol and flavone (TFl) content

The TFl content can be determined using the method described by Kumaran and Karunakaran. To the mixture, add 2 milliliters of the sample, 2 milliliters of a 2% AlCl3 solution in methanol, and 3 milliliters of sodium acetate solution (50 g/L). Incubate the mixture at 20 °C for 2.5 hours, then measure the absorbance at 440 nm.

4.4. Total precipitable alkaloid (TA) content

The TA content could be determined by spectrophotometry and the Dragendorff reagent. Three milliliters of 4% vanillin–methanol (w/v), five milliliters of extract, and Hydrochloric acid, 1.5 milliliters. Let the mixture sit for fifteen minutes. Read the absorption at 500 nm.

4.5. Total proanthocyanidin (TPA) (condensed tannin) content

The method described by Sun et al. (1998) served as the foundation for the TPA content determination. 3 ml of 4% vanillin–methanol (w/v), 1.5 ml of hydrochloric acid, and 0.5 ml of extract were combined. After letting the mixture remain for fifteen minutes, the absorbance at 500 nm was calculated. With the use of the catechin calibration curve (R2 = 0.999),[9].

5. Medicinal uses of N. Sativa:

Previous research has indicated that Nigella sativa seeds exhibit a range of protective qualities against a variety of cancers, including skin, blood, cervical, colon, hepatic, prostate, breast, and renal cancers. Human oxidative stress, hypertension, diabetes, ulcers, epilepsies, fatty liver, asthma, arthritis, inflammatory disorders, and parasite infections have all been successfully treated using Nigella sativa extract, seeds, and oil. [13] Numerous investigations demonstrated the liver toxicity, analgesic, antipyretic, antibacterial, and antineoplastic properties of N. stative seeds. The oil raises hemoglobin, packed cell volume, respiration, and lowers blood pressure, cholesterol, triglycerides, and glucose. N. Sativa seeds have been found to be beneficial in the traditional medical system for treating a variety of conditions, including bronchitis, asthma, dizziness, dysmenorrhea, obesity, hemiplegia, paralysis, back pain, infection, inflammation, rheumatism, and gastrointestinal issues likedyspepsia, dysentery, and diarrhea.

6. Pharmacological activities of Nigella sativaseeds:

6.1. Antibacterial activity:

Many studies on the antibacterial activity of Nigella sativa seeds have been conducted against bacterial species such as Salmonella species, Escherichia coli, Staphylococcus aureus, Pseudomonas aeruginosa, Staphylococcus haemolyticus, Klebsiella pneumoniae, Candida albicans, and Candida glabrata, according to the literature on antibiotic activity. Thus, it is verified by the literature that N. sativa seeds can be used to treat any bacterial disease caused by these kinds of bacteria. [14-15]

6.2. Antifungal activity

In their research, Shady et al. explored the antimicrobial properties of three endophytic fungi isolated from *N. sativa* seeds. The fungi, *Aspergillus* spp. SA1, SA2, and SA3, were tested against several pathogens, including *Candida albicans* (ATCC 10231), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 27853), *Klebsiella pneumoniae* (ATCC 13883), MRSA (ATCC 33591), and *Staphylococcus aureus* (ATCC 9144). The most active fungi were identified through molecular methods, utilizing internal transcribed spacer (ITS) sequencing. A technique guided by HR-ESIMS was effectively used to analyze the chemical profile of 26 bioactive secondary metabolites found in *N. sativa* seeds. These metabolites fall into several categories, such as polyketides, benzenoids, quinones, alcohols, phenols, and alkaloids. In silico studies further suggested that the bacterial DNA gyrase could be a potential target for these antimicrobial compounds, alongside the fungal Cyp51 active site [16]

6.3. Antioxidant activity:

The main component of N. sativa seeds, thymoquinone (TQ), exhibits antioxidant activity,according to research and literature on N. Sativa seeds. The N. sativa seed oil, which has a TQ of roughly 73.48–1.23 mg/kg according to GC-MS analysis, was investigated by S. Warinhomhoun et al. N. sativa seeds contain compounds called flavonoids, which are potent antioxidants. They alsoaid in lessening the body's oxidative stress. [17]

7. Computational approaches:

7.1. Computational approaches of N. Sativa against SARS-CoV-2.

The ability of the main chemical components of N. sativa to bind to the active site of the SARS-CoV-2 virus's RNA-dependent RNA polymerase (RdRp) enzyme was the basis for the study's assessment, carried out by M. Alaidarous et al. Molecular docking techniques were employed in the investigation to evaluate the binding affinity, and the phytochemical interaction with the RdRp receptor activesite has been examined and depicted using the appropriate molecular docking tools. Among the nine N. sativa Chemical constituents that were assessed for this study, four alpha-hederin, dithymoquinone, nigellicine, and nigellidine, exhibited a substantial docking score. The study found that a-hederin is the most effective inhibitor of RdRp of SARS-CoV-2 and has the lowest binding energy (-8.6 kcal/mol) of all the compounds tested [18].

7.2. Computational approaches of N. Sativa against dengue virus:

In order to predict drug likeness, oral bioavailability, and non-toxic and non-mutagenic effects, Mukhtar et al. undertook research that may aid in the development of new, safer medications. The current study aimed to determine if 18 phytochemicals from Nigella sativa could inhibit the dengue virus's two key enzymes, NS2B/NS3 and NS5. Apigenin, taraxerol (−9.1 kcal mol−1), isoquercetin (8.4 kcal mol−1), stigmasterol (−8.3 kcal mol−1), and taraxerol (−9.1 kcal mol−1) have demonstratedencouraging outcomes in NS2B/NS3. In a similar vein, NS5 has shown favourable results with autodock methods for apigenin (−9.9 kcal mol−1), rutin (−9.3 kcal mol−1), nigellicine (−9.1 kcal mol−1), and stigmasterol

(−8.8 kcal mol−1) [19].

7.3. Computational approaches of N. Sativa against COX II:

With the help of several in silico docking methods, five distinct ligands with a more stable association than the first inhibitors were found for every COX-II molecule. Abdelhalim H et al. conducted a study about the interactions between the binding pocket of COX-II molecules and the 23-chemical constituent of N. sativa in order to identify the best compounds for inhibition. [21]

7.4. Computational approaches of N. Sativa against Covid-19:

Through in silico techniques, like molecular docking with many software programs like AUTO DOCK 4.2 and PATCH DOCK, Pandey et al.'s study sheds insight on the inhibitory role of phytocompounds of Nigella sativa against different major targets of coronavirus. Conclusions: By examining the most well-reported phytocompounds from Nigella sativa, we have been able to clarify their potential as strong COVID-19 inhibitors. Our research has mostly concentrated on blocking fourdistinct targets in CoVs. In order to determine which of ten strong chemicals would be the most effective in blocking viral attachment and reproduction, molecular docking was used. With a binding energy of -5.48, nigellone has demonstrated the strongest inhibitory potential against all four of the coronavirus's critical targets. [22].

7.5. Computational approaches of N. Sativa against apoptotic proteins:

Bcl-xL and Mcl-1 are two examples of anti-apoptotic proteins that Oladapo O. et al. studied in searchof powerful novel anticancer targets. This study explores the inhibitory effects of the medicinal herb *Nigella sativa* on various targets through molecular modeling. Based on molecular docking results, seven compounds—apigenin, chlorogenic acid, hesperidin, quercetin, quercitrin, kaempferol, and rutin—are predicted to have stronger inhibitory potential against the target protein, with higher docking scores indicating better binding affinities compared to co-crystallized compounds.

Table 1: Docking scores of some chemical constituents of N. Sativa with Receptors

Sr.no.	Ligand	Receptor	Molecular docking resultKcal/mol	Reference
1	Alpha-hydrine	RdRp (SAR-COV-2)	-8.6	[18]
2	Teraxerol	NS2D/NS3	-9.1	[19]
3	Apigenin	NS5	-9.9	[19]
4	Thymoquinone	5F1A	-7	[21]
5	Nigellidine	5KIR	-8.8	[21]
6	Nigellone	Covid-19	-5.48	[22]
7	Chlorgenic acid	Bcl-x/Mcl-1	-8.3/-11.8	[23]

8. Conclusions

Nigella sativa seeds possess a wide range of active compounds that contribute to their ability to treat various diseases. The most important active components include thymoquinone, thymohydroquinone, dithymoquinone, p-cymene, carvacrol, 4-terpineol, α-pinene, thymol, and sesquiterpene longifolene. The seeds also contain significant alkaloids, such as isoquinoline alkaloids (nigellicimine and nigellicimine N-oxide) and pyrazole alkaloids (nigellidine and nigellicine), which enhance their therapeutic potential. Additionally, Nigella sativa seeds have alpha-hederin, a water-soluble pentacyclic triterpene, and saponins, which are being studied for their potential anticancer properties. Several extraction techniques, including cold extraction, microwave-assisted extraction (MEA), and ultrasonic-assisted extraction (UAE), have been widely used to maximize the yield of these bioactive compounds. These methods are effective in isolating the highest percentage of the seed's chemical constituents. Nigella sativa has demonstrated remarkable medicinal properties, particularly in its ability to combat various types of cancer such as blood, skin, cervical, colon, liver, prostate, breast, and kidney cancers. Beyond cancer treatment, the seed extract, oil, and whole seeds have shown effectiveness in managing conditions like oxidative stress, hypertension, diabetes, ulcers, epilepsy, fatty liver, asthma, arthritis, and inflammatory diseases. Furthermore, Nigella sativa also shows potential in treating parasitic infections. The therapeutic benefits of Nigella sativa can be studied using different in silico or in vivo methods, which may further uncover its full medicinal potential. Overall, the multifaceted health benefits of Nigella sativa make it a valuable natural remedy with applications across many areas of human health.

9. Future aspects: *Nigella sativa* seeds, with their extensive therapeutic properties including antimicrobial, anti-inflammatory, and antioxidant effects, hold significant potential for future pharmaceutical applications. Upcoming research should aim to enhance extraction technologies to yield higher quantities of potent bioactive compounds such as thymoquinone. Additionally, rigorous clinical studies are necessary to establish effective doses for treating conditions like cancer and cardiovascular diseases. There is also scope to explore the plant's application in combating drug-resistant pathogens and boosting immune health. Computational modeling could serve as a powerful tool for identifying new molecular targets, particularly for addressing global health concerns such as COVID-19. These innovations could position *Nigella sativa* as a critical component in integrative medicine, with expanded use in both preventive and curative care.

Abbreviations: N. Sativa – Nigella Sativa, HD – Hydro distillation, MAE - Microwave-Assisted Extraction Method, ASE- Accelerated Solvent Extraction Method, HPLC: High Performance Liquid Chromatography, LC-MS - Liquid Chromatography- Mass Spectroscopy, GC- MS – Gass Chromatography - Mass Spectroscopy, TP- Total Phenolic Content, TFd- Total Flavonoids, TFI – Total Flavonol and Flavone, TA- Total Precipitable Alkaloids, TPA- Total proanthocyanidin,

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