A Review on Pharmacological and Phytochemical Activities of *Lilium polyphyllum* (Liliaceae): Himalaya Lily

Kunal Bera, Parag Ghosh*, Soumyadip Halder, Nilesh Naskar, Subhadip Bhowmik, Susobhan Mondal, Ankita Bairagi, Anjushree Purkait School of Pharmacy, The Neotia University, Jhinga, Sarisa, Diamond Harbour Road, 24 Parganas(South),West Bengal – 743368

Abstract:- Nature has always been a supreme source for many therapeutic compounds yielding us with many microorganisms producing beneficial chemicals and medicinal plants. The herbal or medicinal plant is used to heal & treat different human diseases from ancient times. In the current era, people suffering from numerous diseases and taking synthetic drugs, which show several side effects and damage our precious body by lifethreatening diseases. The main goal of this review article to highlight the different phytochemicals & is pharmacological activities of Lilium polyphyllum based on various scientific literature surveys. The common name of Lilium polyphyllum is "White Himalaya lily" which belongs to the family Liliaceae. It is marked as a precious plant of the Indian system of medicine. It is mainly found in different states of North and West-India, USA, Italy, Russia, UK, France, Spain, Germany, Chinaetc. Phytochemical studies showed that *Lilium polyphyllum* is a rich source of different active chemical constituents like alkaloids, furocoumarins, flavonoids, O-isopentenyl, halfordinol, glycoside, etc. Major pharmacological activities and steroid glycerides presented by this plant are anti-inflammatory activity, anti-tumor, antidepression, anti-bacterial and also used to treat hyperdipsia, haematemesis, intermittent fever, bronchitis, rheumatology& general disability etc. Therefore, it can be concluded that "Lilium polyphyllum" may be considered as a natural source of many pharmacologically active constituents and useful for the development of herbal formulations.

Keywords:- Lilium Polyphyllum, Bronchitis, Anti-Inflammatory, Anti- Bacterial.

I. INTRODUCTION

There are roughly 110 species of herbaceous perennials in the genus Lilium (family Liliaceae), which has been divided into 5-10 divisions or subgenera.[1].Scattered over the northern hemisphere's cold and temperate zone. In Jammu & Kashmir, Himachal Pradesh, and Uttarakhand, it is dispersed sparingly [2]. The genus is significant in the global flower industry because of its diversity and the enormous number of commercially available hybrids and cultivars. However, several species are also valued as foods and medicines [3,4] could greatly boost the economic relevance.

Bulb plants from the genus Lilium, such as L. Polyphemus, L. lancifolium, and L. candidum, have a high therapeutic potential. Bulbs have calming, astringent, and anti-inflammatory qualities in medicine. The remedy is utilized for cough, bronchitis, seminal weakness, strangury, burning feeling intermittent fever, haematemesis, and overall incapacity. It also functions as a refrigerant, galactogogue, expectorant, aphrodisiac, diuretic, antipyretic, and tonic. [5] The bulbs are also utilised in chyawanprash and a night cream that promotes vigour. [5] Raw bulbs are consumed in high altitudes to combat the cold. The species was said to rapidly restore health and act as an antioxidant in the body in conventional medicine. [6] The chemical components of the genus Lilium have been the subject of several research that have demonstrated their pharmacological effects on cancer, diabetes, bacteria, inflammation, blood lipids, depression, tiredness, and hypoxia tolerance. In order to provide a more in-depth understanding of the therapeutic qualities of the plant as a pharmacopoeial species, the review in this work aims to give a thorough and critical evaluation of the chemical. botanical, and pharmacological features of Lilium hybrids.

II. METHOD

In order to find pertinent material, a variety of electronic and scientific search engines and specialized reference tools were employed, including Google Scholar, Web of Science, scientific literature, publishing websites, and electronic databases. In order to gather comprehensive information on the therapeutic applications of the herb liium, a systematic search was also conducted in online research libraries like Elibrary and particular pharmaceutical publications.

III. FINDINGS

A. Botanical Characteristics

From Europe to North Asia, the Liliaceae family of plants includes the Lilium plant. The "white lily" is a herbaceous bulbous perennial plant that can only be found in its natural environment in the Himalayan area. [7] It may be discovered in the high-altitude, arctic regions of Afghanistan, Pakistan, Nepal, and India. [8] For its modest and lovely blossom, the lily species is artificially grown. The ground rosette gives rise to the lance-shaped leaves. Up to 150 cm tall, the stem bears straight, heavily overgrown leaves. The flowers have a lovely scent and can grow up to 10 cm in size. On a single stalk, there might be up to 15 blossoms. In June

ISSN No:-2456-2165

and July blooms fruits come in capsule form. Scale leaves generally grow in concentric layers on bulbs, starting from a basal disc. *L. polyphyllum's* bulb has linalool and -terpineol in it. [9]

B. Composition of Biologically –Active Compounds

There hasn't been much research done on the Lilium's chemical makeup thus yet. Extracts of flowers, roots, and bulbs were used to separate a variety of biologically active compounds. It has been proven that the plant has alkaloids in every section, as well as saponins and flavonoids in the aerial portions. Proteins, vitamins, sugar, and boron are all present in considerable quantities in the bulbs. [10] Mostly the flavonoids (Quercetin, Kaempferol, isorhamnetin,) [11] However, carotenoids, steroidal alkaloids, pyrrole alkaloids (lilalin, jatrophan), steroids (beta-sitosterol), and steroid saponins of the furostane and spinostane types, tannins, polysaccharides, organic acids, and amino acids are some of the other significant bioactive compounds. [12] The members of the genus Lilium provided the steroidal saponin chemicals. [2] From the plants L. candidum and L. longiflorum, respectively, the steroidal alkaloids and further steroid glycoside alkaloids were discovered. [13] According to TLC examination of plants at various vegetative stages (during initial growth period, throughout growth, at the commencement of blooming and flowering stage) in the spring-summer period, the subterranean and aerial sections of the plant collect -methylene glutamic acid at the highest concentration. [14]

C. The pharmaceutical properties of Lilium

The stems, leaves, flowers, and bulbs of Lilium species are utilised as raw materials for pharmaceuticals. The juice of *L. martagon* is used to treat stomach ulcers and exterior wounds. The *L. candidum* is a similarly old plant that is utilised in China as a significant culinary plant and as a significant biomedicine to treat the symptoms of numerous inflammatory diseases in humans [15] and they are grown as decorative plants all throughout the world. Since the dawn of time, this plant has assisted in the treatment of inflammatory and suppurative wounds, ulcers, skin inflammations, burns, and other disorders. [16] The formulations made by *L. Martagon* are used to treat gynaecological illnesses because they contain anti-inflammatory, sedative, analgesic, and hemostatic qualities. Lily bulbs are frequently used as potent anti-hemorrhagics and to cure bladder and rectum discomfort. Gallbladder conditions are treated with the flower infusion. [17] In addition, L. martagon is well known for its usage in the treatment of malignancies. Extracts of L. martagon are helpful for skin whitening and inhibiting melanin formation in the skin's epidermal layers. The medicinal benefits of Lilium are widely recognised as an anti-inflammatory treatment for burns and ulcers, as well as a proven method of delaying the healing of wounds. [18] The anti-inflammatory benefits of lilies are likely caused by a variety of steroids and steroid glycosides. [19] Fresh L. candidum bulb saponins of spirostanol and furostanol were extracted. [20] L. lancifolium root extracts have anti-inflammatory properties. [21] In order to demonstrate the anti-inflammatory impact, the antiinflammatory mechanisms inhibited the generation of inflammatory components. According to these findings, liaoum plants may have therapeutic benefits for the treatment of inflammatory illnesses. In Chinese medicine, the bulbs of Lilium species, such as L. brownii and L. lancifolium, are utilised as anti-tumor herbs. According to the results, [22] L. candidum extracts cause apoptosis to be stimulated, which in turn causes cytotoxicity in human breast cancer cells. According to the study, [23] the polysaccharide and which improves immune function in H22 tumour development may be responsible for the anti-tumor actions. These results demonstrate the possible anti-tumor effects of the crude extracts and certain active components from L. brownii, L. lancifolium, and L. candidum. The L. lancifolium bulb extracts shown strong antioxidant capability and may represent a natural source of antioxidants. According to a research, [15] the phenolic compounds isolated from L. lancifolium bulbs shown potent antioxidant and free radical scavenging properties. The research has demonstrated that the methanol extracts of L. candidum flower contain certain active compounds with the ability to protect the liver. [24] The bulbs of L. davidii, L. leucanthum, L. regale, L. brownii, and L. lancifolium were linked to beneficial compounds such alkaloids, flavanoids, and saponinsbased on their antibacterial action. [25] The antibacterial activity and the components of lily bulb extracts had a strong dosage effect relationship. The findings also indicated that the antibacterial activity rose proportionately as the amount of lily bulb extracts increased. [25]

Compound	Medicinal Uses	References
Kaempferol	Anti-apoptotic, pro-wound healing, anti-cancer, cardioprotective, anti-oxidant, pro-apoptotic, anti-allergic, anti-parasitic, anti- diabetic, anti-adipogenic, anti-thrombotic, anti-inflammatory, anti- metabolic syndrome, anti-bacterial, immunoregulatory, hepatoprotective, anti-atherosclerosis	[26-33]
Linalool	Anti-parasitic, anti-convulsant, anti-cancer, anti-bacterial, neuroprotective, anti-oxidant, anti-inflammatory, anti-Alzheimer, anxiolytic, hepatoprotective, anti-hyperalgesic, neuroprotective	[34-41]
Citronellal	Anti-fungal, insect repellant, hepatoprotective, anti-nociceptive, anti-inflammatory, anti-bacterial	[42-44]
Caryophyllene	Anti-cancer, anti-mutagenic, anti-bacterial, oxygen deprivation protective, neuroprotective, hepatoprotective, anti-convulsant, anti- diabetic, anti-microbial, anti-Alzheimer, pro-longevity, analgesic, nephroprotective.	[45-54]
Humulene	Inseccidal, anti-cancer, anti-inflammatory	[49, 55, 56]
Neridiol	Anti-parasitic, antioxidant, neuroprotective, pro-wound healing, anti-microbial	[57-60]

Table 1:- Phytochemicals found in *Lilium polyphyllum* have medicinal potential.

IV. CONCLUSION

The herbaceous perennial *Lilium*, which has fragrant blossoms, is used in both conventional and contemporary medicine to treat a variety of physiological ailments. A variety of bioactive compounds, including saponins, flavonoids, alkaloids, aminoacids, and polysaccharides, are present in the plant. That has sedative, analgesic, antitumor, anticancer, and anti-inflammatory properties. It is still to be determined the therapeutic effects of many chemically varied substances extracted from *Lilium*, and the mechanism is still being further confirmed. In order for *Lilium* to quickly establish itself as one of the health research oriented programmes, it is necessary to investigate the relationship between the chemical makeup of various bioactive substances found in *Lilium* and their pharmacological effects in healthcare products. Related drugs should also be thoroughly researched.

REFERENCES

- [1]. Mabberley DJ. Mabberleys plant book: a portable dictionary of plants their classification and uses. United States of America by Cambridge university press publishers, New York, 2008.
- [2]. Ved DK, Kinhal GA, Ravikumar K, Prabhakaran V, Ghate U, Vijaysankar R et al. Conservation assessment and management prioritisation for the medicinal plants ofHimanchal Pradesh, Jammu and Kashmir and Uttaranchal foundation of Revitalisation of Local health Traditions, Bangalore, India, 2003.
- [3]. Chang C, Chen CT, Tsai YC, Chang WC. A tissue culture protocol for propagation of a rare plant, LilliumSpeciosum thumb. Var. Glorisoides baker., Bot. Bull. Acacd. Sin. 2000; 41:139-142.
- [4]. Dhayani A. Exploring Liliumpolyphyllum in Uttarakhand, India. The Lily yearbook of North American Lily Society. 2007, 79-82.

- [5]. Rana MS, Samant SS. Population biology of LiliumPolyphyllum D. Don ex Royle-a critically endangered medicinal plant in a protected area of North-Western Himalaya., J Nat. Conserv. 2011; 19(3):137-142.
- [6]. Sharma BD, Balkrishna AV. Vitality strengtheningAstavarga plants (Jeevaniya&b VayasthapanPaudhe).Divya publishers, DivyayogMandir, Haridwar,Uttaranchal, 2005.
- [7]. Rana MS, Samant SS. Threaat categorization an conservation prioritization of floristic diversity in theIndian Himalayan Region- a state of art approach from Manali, wildlife sanctuary., J Nat. Conserv., 2010; 18(3):159-168.
- [8]. Dhayani A, Nautiyal BP, Nautiyal MC. Age determination of the perennial herb Liliumpolyphyllum(Liliaceae). Nor. J. Bot. 2012; 30:503-505.
- [9]. Balkrishna A, Srivastava A, Mishra RK, Patel SP,Vashistha RK, Singh A et al. Astavarga plants-threatened medicinal herbs of the North-West Himalaya. Int. J Med. Arom. Plants. 2012; 2:661-676.
- [10]. Kucherov EV. Wild food plants of Bashkiria and theiruse, 1990, 68-69.
- [11]. Tappi G, Karrer P. Isorhamneinaus den StaubbeuteinVon Liliumcandidum. Helv. Chem. Acta.m. 1949;32(1):32.
- [12]. Haladova M, Buckova A, Eiseenreichova E, Tomko J, Uhrin D. Dimeric pyroline alkaloids from LiliumCandidum L, collect. Czech. Chem. Commun., 1991; 56(2):436-438.
- [13]. Mimaki Y, Satou T, Kuroda M, Sashida Y, Hatakeyaaama Y. Steroidal saponins from the bulbs of Liliumcandidum. Phytochemistry. 1999; 51(4):567-573.
- [14]. Rossetti V. γ- Methyleneglutamic acid in LiliumMartagon. Planta. Med., 1981; 41(02):204-205.

ISSN No:-2456-2165

- [15]. Jin L, Zhang Y, Yan L, Guo Y, NIu L. Phenolic compound and antioxidant activity of the bulb extracts of six Lilium species native to china. Molecules., 2012; 17(8):9361-9378.
- [16]. Pieroni A. Medicinal plants and food medicines in the folk traditions of the upper Lucca Province, Italy., J Ethnopharmacol. 2000; 70(3):235-273.
- [17]. Znamensky IE. Plant raw materials part iv. Wild edible Plants, chemical and technical Reference., 1932, 12.
- [18]. Rasoulinezhad S, Yekta NH, Fallah E. Promising pain relieving activity of an ancient Persian remedy (mixtureOf White Lily in sesame oil) in patients with chronic lowBack pain., J Fam. Med. Prim. Care. 2019; 8(2):634.
- [19]. Munafo JR, Ramanathan JP, Jimenezls A, Giaanfagna TJ. Isolation and structural determination of steroidal glycosides from the bulbs of Easter Lily (LiliumLongiflorumThunb.) J. Agr. Food. Chem., 2010; 58(15):8806-8813.
- [20]. Mimaki Y, Satou T, Kuroda M, SashidaY,Hatakeyaaama Y. Steroidal saponins from the bulbs of Liliumcandidum. Phytochemistry. 1999; 51(4):567-573.
- [21]. Kwon OK, Lee MY, Yuk JE. Anti-inflammatory effects of methanol extracts of the root of Liliumlancifolium., J Ethnoooooopharmocoll., 2010; 130(1):28-34.
- [22]. Tokgun O, Akca H, Mammadov R, Aykurt C, Deni G. Vnvolvulusgulaticus crocks antalyensis and LiliumCandidum extracts show their antitumor activity through induction of P53 – mediated apoptosis on human breast Cancer cell line MCF-7 cells., J Med>Food., 2012; 15(11):1000-1005.
- [23]. Han H, Xie HC. A Study on the extraction and purification process of Lily polysaccharide and its anti-Tumor effect. African. J Trad. Compl. Alter. Med., 2013; 10(6):485-489.
- [24]. Devi NI, Kuar SN, Rajaram C. Evaluation of Hapatoprotective activity of Liliumcandidum L. In experimental models., world. J Pharmaceu. Res. 2016; 5(12):725-749.
- [25]. Tang M. Research on extraction, Purification and activity of Polysaccharides in Lilium. Hunan. Agriculture. University, 2010.
- [26]. Bolaños, V.; Díaz-Martínez, A.; Soto, J.; Marchat, L.A.; Sanchez-Monroy, V.; Ramírez-Moreno, E. Kaempferolinhibits Entamoebahistolytica growth by altering cytoskeletal functions. Mol. Biochem. Parasitol. 2015, 204,16–25. [CrossRef]
- [27]. Choi, J.H.; Park, S.E.; Kim, S.J.; Kim, S. Kaempferol inhibits thrombosis and platelet activation. Biochimie 2015, 115, 177–186. [CrossRef]
- [28]. Devi, K.P.; Malar, D.S.; Nabavi, S.F.; Sureda, A.; Xiao, J.; Nabavi, S.M.; Daglia, M. Kaempferol and inflammation: from chemistry to medicine. Pharmacol. Res. 2015, 99, 1–10. [CrossRef]
- [29]. Hoang, M.H.; Jia, Y.; Mok, B.; Jun, H.J.; Hwang, K.Y.; Lee, S.J. Kaempferol ameliorates symptoms of metabolic Syndrome by regulating activities of liver x receptor-β. J. Nutr. Biochem. 2015, 26, 868–875. [CrossRef]

- [30]. Li, H.; Yang, L.; Zhang, Y.; Gao, Z. Kaempferol inhibits fibroblast collagen synthesis, proliferation and activation in hypertrophic scar via targeting tgf-β receptor type i. Biomed. Pharmacother. 2016, 83, 967– 974. [CrossRef]
- [31]. Shin, D.; Park, S.H.; Choi, Y.J.; Kim, Y.H.; Antika, L.D.; Habibah, N.Y.; Kang, M.K.; Kang, Y.H. dietary compound kaempferol inhibits airway thickening induced by allergic reaction in a bovine serum albumininduced model of asthma. Int. J. Mol. Sci. 2015, 16, 29980–29995. [CrossRef]
- [32]. Suchal, K.; Malik, S.; Gamad, N.; Malhotra, R.K.; Goyal, S.N.; Bhatia, J.; Arya, D.S. Kampeferol protects against oxidative stress and apoptotic damage in experimental model of isoproterenol-induced cardiac toxicity in rats. Phytomedicine 2016, 23, 1401–1408. [CrossRef] [PubMed]
- [33]. Suchal, K.; Malik, S.; Gamad, N.; Malhotra, R.K.; Goyal, S.N.; Chaudhary, U.; Bhatia, J.; Ojha, S.; Arya, D.S. Kaempferol attenuates myocardial ischemic injury via inhibition of mapksignaling pathway in experimental model of myocardial ischemia-reperfusion injury. Oxid. Med. Cell. Longev. 2016, 2016, 7580731. [CrossRef] [PubMed]
- [34]. Alves, S.; Duarte, A.; Sousa, S.; Domingues, F.C. Study of the major essential oil compounds of coriandrumsativum against acinetobacterbaumannii and the effect of linalool on adhesion, biofilms and quorum sensing. Biofouling 2016, 32, 155–165. [CrossRef] [PubMed]
- [35]. Dutra, F.L.; Oliveira, M.M.; Santos, R.S.; Silva, W.S.; Alviano, D.S.; Vieira, D.P.; Lopes, A.H. Effects of linalool and eugenol on the survival of Leishmania (L.) infantumchagasi within macrophages. Acta Trop. 2016, 164,69–76. [CrossRef]
- [36]. Li, X.J.; Yang, Y.J.; Li, Y.S.; Zhang, W.K.; Tang, H.B. A-pinene, linalool, and 1-octanol contribute to the topical anti-inflammatory and analgesic activities of frankincense by inhibiting cox-2. J. Ethnopharmacol. 2016, 179, 22–26. [CrossRef]
- [37]. Mehri, S.; Meshki, M.A.; Hosseinzadeh, H. Linalool as a neuroprotective agent against acrylamide-induced neurotoxicity in wistar rats. Drug Chem. Toxicol. 2015, 38, 162–166. [CrossRef]
- [38]. Park, H.; Seol, G.H.; Ryu, S.; Choi, I.Y. Neuroprotective effects of (-)-linalool against oxygenglucose deprivation-induced neuronal injury. Arch. Pharmacal Res. 2016, 39, 555–564. [CrossRef]
- [39]. Sabogal-Guáqueta, A.M.; Osorio, E.; Cardona-Gómez, G.P. Linalool reverses neuropathological and behavioralimpairments in old triple transgenic alzheimer's mice. Neuropharmacology 2016, 102, 111– 120. [CrossRef]
- [40]. Seol, G.H.; Kang, P.; Lee, H.S.; Seol, G.H. Antioxidant activity of linalool in patients with carpal tunnel syndrome. BMC Neurol. 2016, 16, 17. [CrossRef]
- [41]. Souto-Maior, F.N.; Fonsêca, D.V.D.; Salgado, P.R.R.; Monte, L.D.O.; de Sousa, D.P.; de Almeida, R.N. Antinociceptive and anticonvulsant effects of the monoterpene linalool oxide. Pharm. Biol. 2017, 55, 63– 67.

ISSN No:-2456-2165

- [42]. Du, E.J.; Ahn, T.J.; Choi, M.S.; Kwon, I.; Kim, H.W.; Kwon, J.Y.; Kang, K. The mosquito repellent citronellal directly potentiates drosophila trpa1, facilitating feeding suppression. Mol. Cells 2015, 38, 911.
- [43]. Maßberg, D.; Simon, A.; Häussinger, D.; Keitel, V.; Gisselmann, G.; Conrad, H.; Hatt, H. Monoterpene (–)citronellal affects hepatocarcinoma cell signaling via an olfactory receptor. Arch. Biochem. Biophys. 2015, 566, 100–109. [CrossRef] [PubMed]
- [44]. Singh, S.; Fatima, Z.; Hameed, S. Citronellal-induced disruption of membrane homeostasis in Candida albicans and attenuation of its virulence attributes. Rev. Soc. Bras. Med. Trop. 2016, 49, 465–472. [CrossRef] [PubMed]
- [45]. Basha, R.H.; Sankaranarayanan, C. B-caryophyllene, a natural sesquiterpene lactone attenuates hyperglycPubMe mediated oxidative and inflammatory stress in experimental diabetic rats. Chem. Biol. Interact. 2016, 245, 50–58. [CrossRef] [PubMed]
- [46]. De Oliveira, C.C.; de Oliveira, C.V.; Grigoletto, J.; Ribeiro, L.R.; Funck, V.R.; Grauncke, A.C.B.; De Souza, T.L.; Souto, N.S.; Furian, A.F.; Menezes, I.R.A. Anticonvulsant activity of β-caryophylleneagainst pentylenetetrazol-induced seizures. Epilepsy Behav. 2016, 56, 26–31. [CrossRef] [PubMed]
- [47]. Di Giacomo, S.; Mazzanti, G.; Di Sotto, A. Mutagenicity of cigarette butt waste in the bacterial rePubMedmutation assay: The protective effects of βcaryophyllene and β-caryophyllene oxide. Environ. Toxicol. 2016, 31, 1319–1328. [CrossRef] [PubMed]
- [48]. Fidyt, K.; Fiedorowicz, A.; Strz adała, L.; Szumny, A. B-caryophyllene and β-caryophyllene oxide—Natural compounds of anticancer and analgesic properties. Cancer Med. 2016, 5, 3007–3017. [CrossRef]
- [49]. Govindarajan, M.; Benelli, G. A-humulene and βelemene from syzygiumzeylanicum (myrtaceae) essential oil: Highly effective and eco-friendly larvicides against anopheles subpictus, aedesalbopictus, and culex tritaeniorhynchus (diptera: Culicidae). Parasitol. Res. 2016, 115, 2771–2778. [CrossRef]
- [50]. Govindarajan, M.; Rajeswary, M.; Hoti, S.; Bhattacharyya, A.; Benelli, G. Eugenol, α-pineneand βcaryophyllene from plectranthusbarbatus essential oil as eco-friendly larvicides against malaria, dengue and japanese encephalitis mosquito vectors. Parasitol. Res. 2016, 115, 807–815. [CrossRef]
- [51]. Kelany, M.E.; Abdallah, M.A. Protective effects of combined β-caryophyllene and silymarin against ketoprofen-induced hepatotoxicity in rats. Can. J. Physiol. Pharmacol. 2016, 94, 739–744. [CrossRef]
- [52]. Ojha, S.; Javed, H.; Azimullah, S.; Haque, M.E. Bcaryophyllene, a phytocannabinoid attenuates oxidative stress, neuroinflammation, glial activation, and salvages dopaminergic neurons in a rat model of parkinsondisease. Mol. Cell. Biochem. 2016, 418, 59– 70. [CrossRef] [PubMed]
- [53]. Pieri, F.A.; Souza, M.C.; Vermelho, L.L.; Vermelho, M.L.; Perciano, P.G.; Vargas, F.S.; Borges, A.P.; Da Veiga-Junior, V.F.; Moreira, M.A. Use of βcaryophyllene to combat bacterial dental plaque

formation in dogs. BMC Vet. Res. 2016, 12, 216. [CrossRef] [PubMed]

- [54]. Tian, X.; Peng, J.; Zhong, J.; Yang, M.; Pang, J.; Lou, J.; Li, M.; An, R.; Zhang, Q.; Xu, L. BcaryophylleneProtects in vitro neurovascular unit against oxygen-glucose deprivation and reoxygenation-induced injury. J. Neurochem. 2016, 139, 757–768. [CrossRef]
- [55]. Lan, Y.H.; Wu, Y.C.; Wu, K.W.; Chung, J.G.; Lu, C.C.; Chen, Y.L.; Wu, T.S.; Yang, J.S. Death receptor 5mediated TNFR family signaling pathways modulate γhumulene-induced apoptosis in human colorectal cancer HT29 cells. Oncol. Rep. 2011, 25, 419–424. [PubMed]
- [56]. Rogerio, A.P.; Andrade, E.L.; Leite, D.F.; Figueiredo, C.P.; Calixto, J.B. Preventive and therapeutic antiinflammatory properties of the sesquiterpene α humulene in experimental airways allergic inflammation. Br. J. Pharmacol. 2009, 158, 1074–1087. [CrossRef]
- [57]. Baldissera, M.D.; Souza, C.F.; Grando, T.H.; Moreira, K.L.; Schafer, A.S.; Cossetin, L.F.; da Silva, A.P.; Da Veiga, M.L.; da Rocha, M.I.; Stefani, L.M.; et al. Nerolidol-loaded nanospheres prevent behavioralimpairment viameliorating Na+, K+-ATPase and AChE activities as well as reducing oxidative stress in the brain of Trypanosomaevansi-infected mice. NaunynSchmiedebergs Arch. Pharmacol. 2017, 390, 139–148. [PubMed]
- [58]. Ferreira, M.O.G.; Leite, L.L.R.; de Lima, I.S.; Barreto, H.M.; Nunes, L.C.C.; Ribeiro, A.B.; Osajima, J.A.; Da Silva Filho, E.C. Chitosan Hydrogel in combination with Nerolidol for healing wounds. Carbohydr. Polym. 2016, 152, 409–418. [CrossRef]
- [59]. Javed, H.; Azimullah, S.; AbulKhair, S.B.; Ojha, S.; Haque, M.E. Neuroprotective effect of nerolidolagCrossReneuroinflammation and oxidative stress induced by rotenone. BMC Neurosci. 2016, 17, 58. [CrossRef]
- [60]. Kaur, D.; Pahwa, P.; Goel, R.K. Protective effect of nerolidol against pentylenetetrazol-induced kindling, oxidative stress and associated behavioral comorbidities in mice. Neurochem. Res. 2016, 41, 2859–2867.