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A Review of chemical constituents and traditional usage of Neem plant (*Azadirachta Indica*)Ahmad Eid^{1*}, Nidal Jaradat¹, Nagib Elmarzugi²¹Department of Pharmacy, Faculty of Medicine and Health Sciences, An-Najah National University, Nablus, Palestine. ²Department of Industrial Pharmacy, Faculty of Pharmacy, Tripoli University & National Nanotechnology Project, Biotechnology Research Center, Tripoli, Libya.

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ABSTRACT

It was estimated from World Health Organization (WHO) that most of the world population depends on herbal medicine for their health care. *Azadirachta Indica* A.Juss also known as neem plant is one of the most popular medicinal plants in Asia and Africa which was used from the ancient times for many medicinal purposes. It is used in many traditional remedies because of its richness with biological active constituents. Some of these chemical constituents are Nimbidin, Nimbin, Nimbolide, Gedunin, Azadirachtin, Mahmoodin, Cyclic trisulphide and others which are used as antipyretic, anti-inflammatory, antibacterial, antigastric ulcer, antiarthritic, spermicidal antifungal, antimalarial, hypoglycemic, immunomodulatory, diuretic and antitumour. Traditionally different parts of the plant are used by populations from many countries for the treatment of several diseases such as leprosy, epistaxis, eye problem, elimination of intestinal worms, anorexia, skin ulcers, biliousness, skin diseases like ringworms, burning sensation, wounds and itching. It is also used as analgesic, alternative and curative of fever and urinary disorder. In addition, it is used in the treatment of cough, asthma, phantom tumour, spermatorrhoea, diabetes, blood morbidity, biliary afflictions and many more medicinal values. The present work provides comprehensive information on the traditional use value and the chemical constituent of *Azadirachta Indica* in order to explore the therapeutic potential, highlight the relation between the traditional use value and the chemical constituents and the scientific future research opportunities on *Azadirachta Indica*.

Keywords: *Azadirachta Indica*, Neem, Traditional remedies, Phytochemistry, Pharmacology.

INTRODUCTION

Human society used the medicinal plants to combat diseases, since the dawn of civilization (1). A number of alternative medicine systems exist in the eastern region of the Mediterranean (2). For thousands of years nature has been a source of medicinal agents and based on their uses in traditional medicine an impressive number of modern drugs have been isolated from natural sources (3). In fact, plants are rich source of different types of medicines because they produce a diverse range of bioactive molecules (4). In the pharmaceutical industries natural products play an important role in drug development programs, therefore, over 50% of all modern clinical drugs are of natural product origin (5). In the addition of the importance of synthetic medicinal chemistry, there is huge interest in herbal medicine, there has been a revival of interest in herbal medicines to control major diseases and to

discover new molecular structures as lead compounds from the plant kingdom (6).

Azadirachta indica A.Juss. Arabic names are nim and nem while the English names are Persian liac, neem tree, bastard tree, Indian liac, bead tree, margosa tree, cornucopia and Indian cedar. This plant described in 1830 by De Jussieu (7) and taxonomically classified as shown in table 1 (8).

Table(1): Classification of Neem plant (51).

Kingdom	Plantae
Phylum	Vascular plant
Class	Magnoliopsida
Order	Rutales
Suborder	Rutinae
Tribe	Melieae
Family	Meliaceae
Subfamily	Melioideae
Genus	<i>Azadirachta</i>
Species	<i>Indica</i>

Azadirachta indica A. Juss. is a tree of small to medium-sized around 18 m, tall up to 15-30 m, with large crown up to 10-20 m diameter (9). The leaves are light green simply pinnate alternate with 20-40 cm long. The flowers are pentamerous, small, white or pale yellow, slightly sweet and bisexual. The plants fruits are greenish yellow to yellow or purple and have one or two seeded drupe, ellipsoidal, 1-2 cm long. They are greenish when ripe and their seeds are ovoid or spherical (10). Neem's leaves, seeds, bark, roots, fruits and oil have become a cynosure of modern medicine and used medicinally for treatment various diseases specially in Indian Ayurvedic medicine, Homoeopathic medicine and Unani (11).

This plant was used for centuries by many cultures for their medicinal values. The advantages of this plant (very popular in many Asian and African countries) are easily available, cheap and low toxicity (12). *Azadirachta indica* is commonly known as Neem. It has great medicinal values and distributed widespread in the world. It is native of India and naturalized in most of tropical and subtropical countries. Their uses and attribution as one of medicinal plants is due to its various different active compounds which can be extracted from each of its parts (13, 14). This review stated a detailed description on the existing chemical constituents and traditional uses of *Azadirachta indica* (neem) tree.

Method of Data Extraction

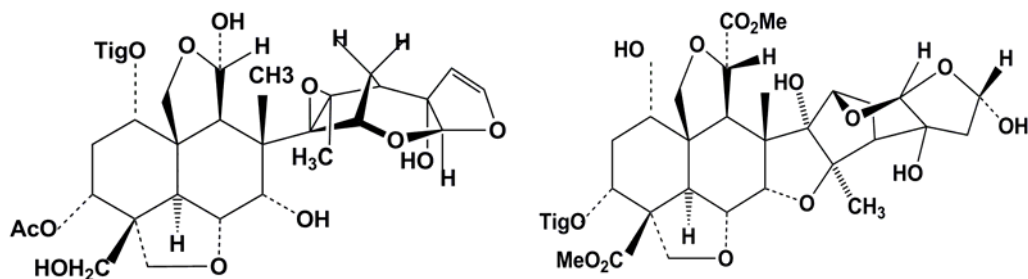
The procedure of collecting the available information on *Azadirachta indica* was via library search for articles published in peer-reviewed journals and ethnobotanical textbooks, as well as via electronic search (using Google Scholar, Pubmed, Web of

Science, Scopus, and other web search engines).

Chemical Constituents

Neem (*Azadirachta indica*) elaborates a vast array of biologically active compounds which are structurally complex and chemically diverse (15, 16). Every part of this plant is used as herb.(13, 17). During the past two decades, the chemical constituents and biological activities of *Azadirachta indica* were intensively investigated in both developing and developed countries. Several published studies revealed a lot of biological compounds (Azadirachtin M and Azadirachtin N) and effects of these compounds on insects, and other inhibitory activities such as antitypanosomal and antiprotozoal (18, 19). Siddiqui et al., (2009) extracted different constituents from the flowers of *Azadirachta indica* and analyzed their insecticidal activity, they found around 38 compounds in the flowers with insecticidal activity (such as: n-Hentriacontane, n-Nonacosane, n-Pentacosane, 2-Methoxy-5,40-dimethylbenzenebutanal, Methyl octadecanoate acid, etc) (20). The group of tetranortriterpenoids, especially azadirachtin analogues is responsible for most of the active principles as it has many antiinfective and antimicrobial properties (21).

The extracted chemical constituents of different parts of neem tree contained many biologically active compounds, including triterpenoids, alkaloids, phenolic compounds, flavonoids, carotenoids, ketones and steroid. The most biologically active compound is azadirachtin. This compound belongs to the C-seco limonoids which was classified as tetranortriterpenes (22). It is actually a mixture of seven isomeric compounds labelled as azadirachtin M and azadirachtin N (Figure 1).

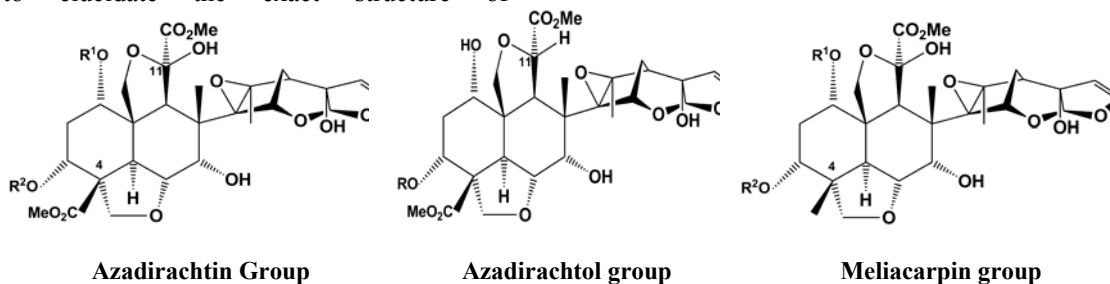


Figure(1): Two novel compounds of azadirachtin analogues collected from seed kernels of *Azadirachta indica*: Azadirachtin M (1) was identified as 29-oxymethylene-11-demetoxy carbonyl-11 α -hydroxyazadirachtin, Azadirachtin N (2) was identified as 22,23-dihydro-23 α -hydroxy-3-tigloyl-11-deoxyazadirachtinin (19). (ChemDraw Ultra 12.0).

These two compounds is more effective and play major role in medicinal activities when compared against second-instar larvae (L2) of *Plutella xylostella* L (23).

The structure of chemical compounds of *Azadirachta indica* is complex. Therefore, many years of study and research were done to elucidate the exact structure of

azadirachtin. In 1968 Azadirachtin was first isolated by Butterworth and Morgan (24). Since that, more than 100 related compounds had been isolated from the neem tree, and these could be assigned to one of three groups: azadirachtols, azadirachtins, and meliacarpins (Figure 2) (25, 26).

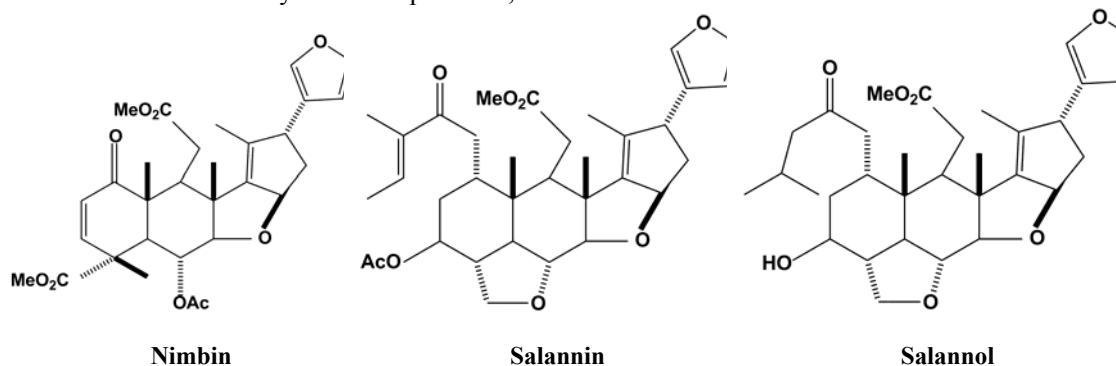


Figure(2): Three groups of natural products isolated from the neem tree. (ChemDraw Ultra 12.0).

The Neem oil comprised of the bitter principles which was formed from biologically active compounds that were isolated from different parts of the plant including meliacin, azadirachtin, gedunin, nimbidin, nimbolides, nimbin, salanin, meliacin and valassin (27). Besides, the seeds also contains tignic acid responsible for the distinctive odour of the oil (17, 28). Around 30-50 % of the oil was extracted from neem kernels. This oil mainly used as pesticide,

soap and by pharmaceutical industries and contain many active ingredients which are together called triterpene or limonoids (29).

The four best limonoids compounds were included Azadirachtin, Salannin, Meliantriol, and Nimbin. Limonoids contain insecticidal and pesticidal activity (30) which lead to its role as an antifeedants, repellents, growth inhibitors, attractants, chemosterilants or as insecticides (Figure 3) (14, 31).



Figure(3): Some of the limonoid compounds isolated from *Azadirachta indica*. (ChemDraw Ultra 12.0).

The phytochemistry screening of Neem samples from leaves extracts also revealed some different chemical constituents compared to other plant parts. The obtained results showed the presence of tannins,

saponins, flavonoids, alkaloids, glycosides, reducing sugars, polyphenols, HCN and terpenes in the ethanolic leaf extract (32, 33). The ethanolic extract of neem's leaves was also showed the composition of fibres,

vitamins and micronutrients. The study proved that *A. indica* contains high fibre content which was $20.11 \pm 0.45\%$, but low protein composition which is $13.42 \pm 0.12\%$ (32).

Apart from that, the investigation of the chemical composition of essential oil isolated from leaves was further analyzed using GC/MS. Analysis of volatiles of leaves was determined that thirty two compounds were identified, which represented 84.98 % of total oil. The oil contains ketones, terpenes and phenolic esters (17).

TRADITIONAL USES

In many parts of the world, the herbal remedies from medicinal plants are used traditionally, but their access to formal healthcare are limited (34). World Health Organization (WHO) has estimated that as many as 80% of world's population rely on herbal traditional medicines as their primary health care (34). This means that the use of natural products as medicine has been widely practiced through folklore from ancient time in world up to now (35, 36). Over 3000 years the neem tree is well known in India and its neighboring countries. It was one of the most versatile medicinal plants having a wide spectrum of biological activities and the following are the commonly used forms of the plant in more than 50 countries. The tree parts are used against various human ailments as traditional medicine for household remedy (12, 37). This tree was usually used as natural pesticide, planting and afforestation as shade trees and to protect against erosion, and definitely as medicinal plants (38).

Azadirachta indica is a very useful traditional medicinal plant in the African sub-continent. Each part of the tree has some medicinal properties which can be used to treat several of diseases (39, 40). The plant is widely cultivated in Nigeria as a decorative and medicinal plant. However, it is quite native to Asia, but has now naturalized in West Africa. It is used extensively in Nigeria for the traditional treatment of malaria and other associated conditions in form of consumption with unspecified quantities without due regards to its toxicological and other adverse effects. This way of

consumption is termed as decoction (41). Based on this traditional and other uses of *Azadirachta indica*, a lot of studies was conducted to ascertain its potentially pharmacologically active components and pharmacological activities (33, 42).

Pakistan as most developing countries has a valuable heritage of herbal remedies (43). Its rural population still depends on the indigenous system of medicine to a great extent that is because herbal medicines have the advantages of being readily available and economical. In addition, the local practitioners claim that these remedies frequently have fewer side effects. Therefore, because some of herbal drugs are commonly used by traditional practitioners, it was considered to be of interest to evaluate and determine the efficacy of for their antipyretic effects (44). Besides its therapeutic efficacies, neem has already established its potential as a source of naturally occurring pesticide, insecticide, and agrochemicals as it showed oviposition deterrence, antifeedant effect on larvae, and toxicity to eggs and larvae of the beet armyworm (45).

In India, the Neem tree twigs are commonly used to scrub teeth. Moreover, the neem tree branches are used as one of the most effective forms of dental care in traditional medicines; even though, it seems a little bit unpleasant for the users (46). Interestingly, the neem trees are an excellent alternative for modern tooth care products. Besides, the leaves of the neem tree are also used as natural treatment for acne sufferers (47). Similarly, treatment of infected eyes can be carried by the use of neem leaves. A similar infusion can also be used in the treatment of sore throats (12).

All parts of neem trees including leaves, seeds, roots, bark and the flowers of the plant are used to cure different ailments, such as stomach ulcers, jaundice and to overcome a variety of infectious and parasitic diseases, ranging from leprosy, chicken pox, and malaria. Infusions and teas made from leaves are used to alleviate malaria attacks, intestinal complaints, treat dental, headache, stimulating the appetite, heartburn and as insects repellent, in addition to that it was also used as a diuretic and for diabetes, also other febrile illnesses as well as to treat

numerous skin diseases (48). The use of aqueous extracts from seeds to treat head lice is widely known. Neem oil showed good antiseptic properties. It is applied in the treatment of such skin complaints as furuncles and eczema, as well as to relieve intestinal worm infections (38). Apart from that, neem-based products from *Azadirachta indica* are traditionally used for pest control in agriculture and gardening since long in India (49, 50).

CONCLUSION

Historical evidences showed the relation between humankind and neem tree and also it showed neem application in health care systems from ancient times to the modern medicine. It has portraits a clear description of neem tree and its broad biopotential activity. It has provided a new vision into the exploration and utilization of neem tree as a source for development of new therapeutic molecules.

CONFLICT OF INTERESTS

The authors report no conflicts of interest in this manuscript

REFERENCES

- 1) Xue CC, Zhang AL, Lin V, Da Costa C, Story DF. Complementary and alternative medicine use in Australia: a national population-based survey. *J Altern Complement Med.* 2007;13(6):643-50.
- 2) Gilani AH. Trends in ethnopharmacology. *J Ethnopharmacol.* 2005;100(1):43-9.
- 3) Tian R-t, Xie P-s, Liu H-p. Evaluation of traditional Chinese herbal medicine: Chaihu (*Bupleuri Radix*) by both high-performance liquid chromatographic and high-performance thin-layer chromatographic fingerprint and chemometric analysis. *J Chromatogr A.* 2009;1216(11):2150-5.
- 4) Krishnaiah D, Sarbatly R, Nithyanandam R. A review of the antioxidant potential of medicinal plant species. *Food Bioprod Process.* 2011;89(3):217-33.
- 5) Kingston DG. Modern natural products drug discovery and its relevance to biodiversity conservation. *J Nat Prod.* 2010;74(3):496-511.
- 6) Ji H-F, Li X-J, Zhang H-Y. Natural products and drug discovery. Can thousands of years of ancient medical knowledge lead us to new and powerful drug combinations in the fight against cancer and dementia? *EMBO Reports.* 2009 02/20;10(3):194-200. PubMed PMID: PMC2658564.
- 7) Jussieu A. Mémoire sur la famille de Myrsinacées. *Mém Mus Natl Hist Nat.* 1830;19:133.
- 8) The Plant List.: The Plant List. Org. Version 1.1.; cited 22.10.2014. Available from: <http://www.theplantlist.org/tpl1.1/record/kew-2667002>.
- 9) Morgan ED. Azadirachtin, a scientific gold mine. *Bioorg Med Chem.* 2009;17(12):4096-105.
- 10) Khare CP. Indian medicinal plants: an illustrated dictionary: Springer; 2007.
- 11) Tiwari R, Verma AK, Chakraborty S, Dhama K, Singh SV. Neem (*Azadirachta indica*) and its potential for safeguarding health of animals and humans: A review. *J Biol Sci.* 2014;14(2):110-23.
- 12) Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and medicinal properties of neem (*Azadirachta indica*). *Curr Sci.* 2002;82(11):1336-45.
- 13) Seddiek SA, Khater HF, El-Shorbagy MM, Ali AM. The acaricidal efficacy of aqueous neem extract and ivermectin against *Sarcoptes scabiei* var. *cuniculi* in experimentally infested rabbits. *Parasitol Res.* 2013;112(6):2319-30.
- 14) Hashmat I, Azad H, Ahmed A. Neem (*Azadirachta indica* A. Juss)-A nature's drugstore: an overview. *Int Res J Biol Sci.* 2012;1(6):76-9.
- 15) Kaur G, Sarwar Alam M, Athar M. Nimbidin suppresses functions of macrophages and neutrophils: relevance to its antiinflammatory mechanisms. *Phytother Res.* 2004;18(5):419-24.
- 16) Koul O, Multani JS, Singh G, Daniewski WM, Berlozecki S. 6 β -Hydroxygedunin from *Azadirachta indica*. Its potentiation effects with some non-azadirachtin limonoids in neem against lepidopteran larvae. *J Agric Food Chem.* 2003;51(10):2937-42.

- 17) Pandey IP, Ahmed SF, Chhimwal S, Pandey S. Chemical Composition and Wound healing activity of Volatile oil of Leaves of *Azadirachta indica* A. juss. *Adv Pure Appl Chem.* 2012;1(3):62-6.
- 18) Ngure RM, Onger B, Karori SM, Wachira W, Maathai RG, Kibugi J, et al. Anti-trypanosomal effects of *Azadirachta indica* (neem) extract on *Trypanosoma brucei rhodesiense*-infected mice. *Eastern J Med.* 2013;14(1):2-9.
- 19) Luo X, Ma Y, Wu S, Wu D. Two novel azadirachtin derivatives from *Azadirachta indica*. *J Nat Prod.* 1999;62(7):1022-4.
- 20) Siddiqui BS, Ali ST, Rajput MT, Gulzar T, Rasheed M, Mehmood R. GC-based analysis of insecticidal constituents of the flowers of *Azadirachta indica* A. Juss. *Nat Prod Res.* 2009;23(3):271-83.
- 21) Kusari S, Verma VC, Lamshoef M, Spiteller M. An endophytic fungus from *Azadirachta indica* A. Juss. that produces azadirachtin. *World J Microbiol Biotechnol.* 2012;28(3):1287-94.
- 22) Ley SV. Development of methods suitable for natural product synthesis: The azadirachtin story. *Pure Appl Chem.* 2005;77(7):1115-30.
- 23) Verkerk RH, Wright DJ. Biological activity of neem seed kernel extracts and synthetic azadirachtin against larvae of *Plutella xylostella* L. *Pestic Sci.* 1993;37(1):83-91.
- 24) Butterworth JH, Morgan E. Isolation of a substance that suppresses feeding in locusts. *Chem Commun.* 1968 (1):23-4.
- 25) Turner CJ, Tempesta MS, Taylor RB, Zagorski MG, Termini JS, Schroeder DR, et al. An NMR spectroscopic study of azadirachtin and its trimethyl ether. *Tetrahedron.* 1987;43(12):2789-803.
- 26) Veitch GE, Pinto A, Boyer A, Beckmann E, Anderson JC, Ley SV. Synthesis of natural products from the Indian neem tree *Azadirachta indica*. *Org Lett.* 2008;10(4):569-72.
- 27) Amitava G, Piyali C, Partha R, Somnath B, Tanushree N, Simli S. Bioremediation of heavy metals from neem (*azadirachta indica*) leaf extract by chelation with dithizone. *Asian J Pharm Clin Res.* 2009;2(1):87-92.
- 28) Pankaj S, Lokeshwar T, Mukesh B, Vishnu B. Review on neem (*Azadirachta indica*): Thousand problems one solution. *IRJP.* 2011;2(12):97-102.
- 29) Djenontin Tindo S, Amusant N, Dangou J, Wotto D, Avlessi F, Dahouénon-Ahoussi E, et al. Screening of Repellent, Termiticidal and Preventive activities on Wood, of *Azadirachta indica* and *Carapa procera* (Meliaceae) seeds oils. *ISCA J Biological Sci.* 2012;1(3):25-9.
- 30) Debashri M, Tamal M. A Review on efficacy of *Azadirachta indica* A. Juss based biopesticides: An Indian perspective. *Res J Recent Sci.* 2012;1(3):94-9.
- 31) Klocke J. Plant compounds as source and models of insect-control agents. research Eamp, editor. London: Academic Press; 1989. p. 103-44.
- 32) Atangwho I, Ebong P, Eyong E, Williams I, Eten M, Egbung G. Comparative chemical composition of leaves of some antidiabetic medicinal plants: *Azadirachta indica*, *Vernonia amygdalina* and *Gongronema latifolium*. *Afr J Biotechnol.* 2009;8(18):4685-9.
- 33) Imothy S, Goji S, Abdussalam B, Mava Y, Galadima I. Antibacterial and phytochemical screening of the ethanolic leaf extract of *azadirachta indica* (neem) (meliaceae). *Int J Appl Biol Pharm Technol.* 2(3):194-9.
- 34) (WHO) WHO. General guidelines for methodologies on research and evaluation of traditional medicine. 2001.
- 35) Dias DA, Urban S, Roessner U. A historical overview of natural products in drug discovery. *Metabolites.* 2012;2(2):303-36.
- 36) Gurib-Fakim A. Medicinal plants: traditions of yesterday and drugs of tomorrow. *Mol Aspects Med.* 2006;27(1):1-93.
- 37) Dev S. Ancient-modern concordance in Ayurvedic plants: some examples. *Development of Plant-Based Medicines: Conservation, Efficacy and Safety:* Springer; 2001. p 47-67.
- 38) Forster P, Moser G. Status report on global neem usage: *Deutsche Gesellschaft für Technische Zusammenarbeit (GTZ).* Eschborn, Germany 2000; p 122.

- 39) Shahed S, Ahmed F, Saha SK, Das SC, Bachar SC. Evaluation of Brine shrimp lethality and Antimicrobial activity of *Azadirachta indica* leaf extract on some drug resistance bacteria in Bangladesh. *Pharmacognosy J.* 2011;3(20):66-71.
- 40) Velusamy P, Das J, Pachaiappan R, Vaseeharan B, Pandian K. Greener approach for synthesis of antibacterial silver nanoparticles using aqueous solution of neem gum (*Azadirachta indica* L.). *Ind Crops Prod.* 2015;66:103-9.
- 41) Katsayal U, Nadabo Y, Isiorho V. Effects of Methanol Extract Of *Azadirachta Indica* Leaves On The Histology Of Liver And Kidney Of Wistar Rats. *Nig J Pharma Sci.* 2008;7(1):9-14.
- 42) Talpur AD, Ikhwanuddin M. <*Azadirachta indica* (neem) leaf dietary effects on the immunity response and disease resistance of Asian seabass, *Lates calcarifer* challenged with *Vibrio harveyi*. *Fish Shellfish Immunol.* 2013;34(1):254-64.
- 43) Ahmed M, Khan MA, Zafar M, Sultana S. Treatment of common ailments by plant-based remedies among the people of district Attock (Punjab) of Northern Pakistan. *Afr J Tradit Complement Altern Med.* 2007;4(1):112-20.
- 44) Khattak SG, Gilani SN, Ikram M. Antipyretic studies on some indigenous Pakistani medicinal plants. *J Ethnopharmacol.* 1985;14(1):45-51.
- 45) Brahmachari G. Neem—an omnipotent plant: a retrospection. *Chembiochem.* 2004;5(4):408-21.
- 46) Prashant G, Chandu G, Murulikrishna K, Shafiulla M. The effect of mango and neem extract on four organisms causing dental caries: *Streptococcus mutans*, *Streptococcus salivarius*, *Streptococcus mitis*, and *Streptococcus sanguis*: An in vitro study. *Indian J Dent Res.* 2007;18(4):148-51.
- 47) Bhowmik D, Yadav J, Tripathi K, Kumar KS. Herbal remedies of *Azadirachta indica* and its medicinal application. *J Chem Pharm Res.* 2010;2(1):62-72.
- 48) Sujarwo W, Keim AP, Caneva G, Toniolo C, Nicoletti M. Ethnobotanical uses of neem (*Azadirachta indica* A. Juss.; Meliaceae) leaves in Bali (Indonesia) and the Indian subcontinent in relation with historical background and phytochemical properties. *J Ethnopharmacol.* 2016;189:186-93.
- 49) Habluetzel A, Lucantoni L, Esposito F. *Azadirachta indica* as a public health tool for the control of malaria & other vector-borne diseases. *Indian J Med Res.* 2009;130(2):112-4.
- 50) Vietmeyer ND. Neem: a tree for solving global problems. Report of an ad hoc panel of the Board on Science and Technology for International Development 1992.
- 51) Girish K, Shankara Bhat S. Neem—a green treasure. *Electron J Biotechnol.* 2008;4(3):201-111.