Synthesis Bioactivity and Characterization of Substituted Naphthalenes and their Derivatives - an Overview

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***Abstract*—Recently in biological chemistry, there is a highest demand to develop new drugs from novel organic compound naphthalene and its derivatives. These drugs are involved in various biological activities like anti-fungal, anti-viral, anti-bacterial, anti-oxidant, anti-inflammatory, cytotoxic effects etc. Many previous studies show influence of several aryl derivatives of naphthalene and heteroryl derivatives of naphthalene on their bioactivities, these compounds involved to curve many diseases, which is caused by pathogens. Conjugated naphthalene and their derivatives shows improved biological activities of the parent compound. The main scope of my work is the studies of naphthalene and their derivatives in such a response to develop, design and identify potent drugs, which cures many diseases with little side effects.**

***Index Terms*—Naphthalene derivatives, Aryl compounds, Heteroaryl compounds, Anti-fungal Anti-bacterial, cytotoxic, Anti-viral, Anti-oxidant, Anti-cancer etc.**

I. INTRODUCTION

Most heterocyclic compounds show anti=-microbial properties, hence, used in various sectors like, medicinal, pharmaceutical, agriculture, biological etc. These compounds either natural products and synthesis or derived products. Heterocyclic compounds and their derivatives show platform of medicinal biological, chemical and pharmaceutical research. The most vital activity of the heterocyclic compounds to serve reactive pharmacophores and Biomimetic properties, which is key ingredients of numerous drugs. Heterocyclic compounds like purines, Pyrimidines and their derivatives participate in biological activity in the living beings dyes like Indio strychnine and pigment-like hemoglobin, myoglobin, chlorophyl possess heterocyclic rings many vitamins, some anti-biotic, some amino acids like tryptophan, proline etc., possess heterocyclic compounds. Heterocyclic compounds possess oxygen, Sulphur, nitrogen etc, are very importance to the scientific researchers because, these compounds show medicinal, agricultural, biological, pharmaceutical, veterinary activities, hence, used in corresponding sectors. Recently most heterocyclic compounds researches and found to be possess potent anti-microbial properties.

Benzothiazole, benzoxazole, Benzimidazole, quinoline etc, shows biological activity, these compounds show divers chemical activity and biological activity.

Heterocyclic compounds like sildenafil as Viagra, allopurinol as a gout therapeutic agent, abacaviras an anti-HIV agent, tubers din as an anti-cancer agent, Acyclovir as an anti-viral agent etc, are used in pharmaceutical building units.

Benzo fused azoles are most important heterocyclic compounds, which is building blocks in therapeutically and biologically active compounds. The structure of heterocyclic compounds studies shows important relations to the biological activities the change of substituent groups in the heterocyclic ring system. Shows changes in the biological activities such as anti-fungal, anti-bacterial, anti-virals, anti-ulcer, anti-hypertensive, anti-cancer and anti-histamines, Benzo-1,63-diazole and their derivatives possess important applications in medicinal fields.

Heterocyclic aromatic compounds like benzimidazole and their derivatives are fused compounds. These compounds possess basic as well as acidic properties, and capacity to form salts. These compounds are important and useful in pharmaceutical as well as biological sectors used as pro drugs and in modern

drug synthesis.

Thinbendazole, flubendazole, omeprazole, lansoprazole etc. are benzimidazole base drugs used in various diseases. Heterocyclic compounds possess wide range of biological activities and medicinal activities; hence, its synthesis is very important to the chemists and researchers, which develops new drugs, possess versatile bioactivities.

Naphthalene is an aromatic compound, in which two benzene rings are fused. It is colorless crystalline solid and soluble in organic solvents like CH_2Cl_2 and Cd_4. It is used in insert repellent.

Naphthalene and their derivatives are found naturally synthesized industrially, which possess potent biological activities, hence used in to cure many diseases. Some eg.- are tolnaftate, terbinafine, nafacillin, niftifine etc. these drugs having anti-microbial properties described by several researcher.

Conjugated aryl or Heteroaryl compounds fused with naphthalene and their derivatives shows anti-bacterial activity, which shows drug resistant characters. Ashraf et al. synthesized many indoles which conjugate with naphthalene possess anti-bacterial activity and used for staphylococcus species.

Chopra et al. synthesized naphthylamine derivatives which conjugate with substituted azetidin-2-one. These compounds were effective against several bacterial species like E. coli, P. aerogenosa, B. subtilis, Staphylococcus species etc.

Hydrazine derivatives conjugated with naphthalene were very effective against Gram-positive bacterial and also for, Gram-negative bacterial, synthesized by Sivasankari and Mary.

Naphthalene-piperazine conjugates were synthesized by Kumar et al, which effective against both Gram-positive and Gram-negative bacteria.

Zangade et al, synthesized naphthalene-flavone conjugates, which were effective against several species of bacteria.

Naphthalene-pyrazoline conjugates were synthesized by Azarifar and Shabanzadeh which were effective against several pathogenic strains of bacteria.

It is similar way Kara et al, synthesized phenylamino-thionaphthaquinone, Shakh et al, synthesized 1,4 naphthoquinone conjugate with 1,2,4-triazole-3-thiones were very effective against several bacterial species.

Chopra et al, synthesized naphthalene-thiozolidione adduct were examined and found to be anti-fungal activity and mainly used for candida species.

Ghiya and Joshi synthesized naphthalene conjugates via a one pot green synthetic method. Mixing of substituted aromatic carbonyl compounds with naphthalene-1-Sulfonohydrazide this compound is effective against aspergillus species, using potato-dextrose agar and fluconazole as nutrients and drugs respectively.

Ryu and Chae synthesized several series of naphthalene-based compounds included 2-arylamino-5-hydroxy-naphthalene-1,4-dione, 2-arylamino-3-chloro-5-hydroxy-naphthalene-1,4-dione, 3-arylamino-5-methoxy-naphthalene-1,4-dione etc. These compounds were effective against candida species.

Several attempts conducted to separate naphthalene products from natural sources, which shows biological active agents. Elansary et al, isolate bis-naphthoquinone from ceratostigmaplumbaginoides (hardy blue-flowered lead word) which is secondary metabolite acts as anti-fungal agents against candida albicans.

Similarly Conjugating naphthoquinone with anthraquinone was isolated from bark of Newbouldia laevis plant, which was to be anti-fungal agent.

Campo et al, isolate and identify three pyrans-naphthoquinone from cipurapaludosabulbs, which shows anti-fungal activity. Naphthalene and its conjugates also show anti-inflammatory activity. Muralidharan et al, synthesized number of series of naphthalene-pyrimidine conjugates, which shows anti-inflammatory action.

Naproxen is propionic acid group of NSAID's this naphthalene conjugates shows anti-inflammatory activity.

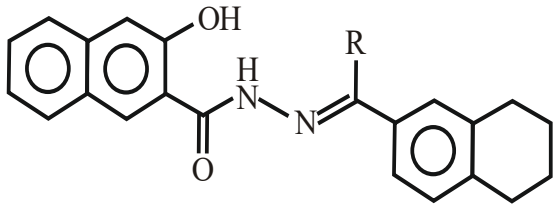
El-Husseiny et al, studies different aryl and heteroryl compounds fused with naproxen, and shows potent anti-inflammatory agents.

Gangwar et al, synthesized thiazolidinone and their derivatives and shows anti-inflammatory activity.

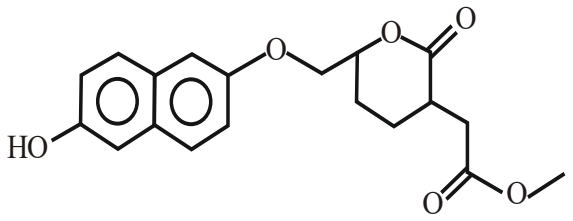
Natural naphthalene-based plant products are investigate and found to be biological properties including anti-inflammatory effect. Tan et al isolate and characterized spiro-bis-naphthalene conjugates from plant originated fungi Edeniagomez pompae, these compounds show anti-inflammatory activity.

Jin et al, Synthesized evaluate and characterized naphthalene-chalcone conjugate, and shows anti-

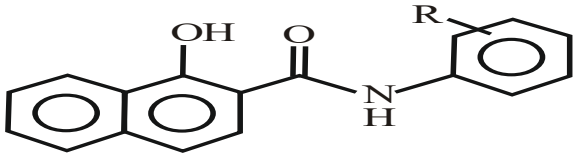
inflammatory activity against several body functions.
Pandey et al, synthesized naphthalene-pyrazole conjugates and shows their anti-inflammatory actions.
Virus is a deadly micro-organism causes several diseases affecting living beings. Naphthalene and their derivatives studied by several researchers and shows their anti-viral properties. Barman et al, conjugate naphthalene-based compound, which fused with tetrahydronaphthalene via a carbohydrazide link, and shows their anti-viral activity against influenza virus.



Perrone et al, synthesized novel anti-viral agents, which is composed of naphthalene and their derivatives, conjugate with aromatic ring and target G4 protein, effective in HIV-1 virus.
Gonzaga et al, synthesized many bis-naphthaquinone-based compounds, and shows anti-zika virus activity.
Wei et al, isolate natural plant originated aryltetrahydronaphthalene compound from phyllanthus niruri leaves, this compound shows anti-hepatitis B virus activity.
Cancer is deadly disease presently worldwide deaths of human beings is due to cancer oncogenes are responsible for cancer growth. Lung, breast and colorectal cancers are the most common cancers in the term of mortality cases. Naphthalene and their derivatives were examined against cancer, Naphthaquinone is the main natural core structure of three natural cytotoxic drugs like daunorubicin, mitoxantrone and doxorubicin. These natural compounds are killers of tumorous cells. Naphthalene-chalcone conjugates substituted with phenyl group is the anti-cancer agents, synthesized by Buddiraja et al, these compounds were tested against ovarian cancer, prostate cancer, liver cancer, neuroblastoma cancer etc.
Rajabi et al, synthesized naphthalene butyrolactone-based conjugated products, used in the treatment of breast cancer and colon cancer.

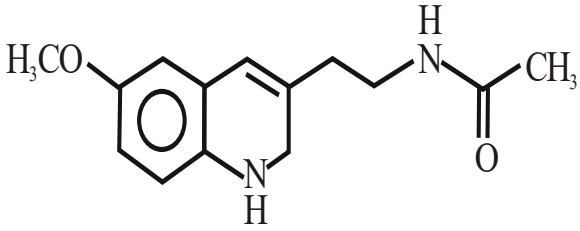


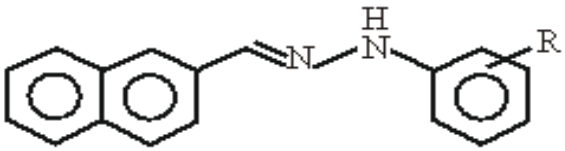
Spaczymskae et al, synthesized many naphthalene-based conjugates and found to be very effective against cancer cells. Cl, Br, NO_2, CF_3 or OCH_3 groups influences the activity of conjugate compounds.



R = Cl, Br, NO_2, CF_3 or OCH_3 group

Karakurt et al. synthesized naphthalene-pyrazole conjugates and it was found to be very effective in tumors cells.
Naphthalene-thiazole-pyrazole comjugates was synthesized by Yuan et al, and investigated their anti-cancer activity.
Wang et al. synthesized many naphthalene-indole conjugate via chalcone linker and shows their cytotoxic activity against various kinds of cancers.
Altin top et al, synthesized naphthalene-based semicarbazones and shows their cytotoxic properties.
Naphthalene and their derivatives also possess anti-oxidants property and fights with different types of human diseases.
Ates-Alagoz et al, synthesized derived compounds of 6-fluoro-5-substituted benzimidazole, in which the 1,1,4,4-tetramethyl-1,2,3,4-tetrahydronaphthalene structure was substituted to the position 2 of the compound benzimidazole ring. These compounds possess good superoxide-anion scavenging property, hence, behaves as an excellent anti-oxidant agent.
Shirinzadeh et al, synthesized many melatonin bio-isosteres, and shows their anti-oxidant activity.





R = H, Br, F, Cl or CH_3

Naphthalene-pyrazolopyridien conjugates were synthesized by Hamdy et al, and shows their anti-oxidant behaviours.

Naphthalene-imidazole conjugate were synthesized by Soma Shekara B et al, and examined their anti-oxidant properties.
Benzothiophene-naphthoquinone conjugate were synthesized by Gouda et al and investigated their anti-oxidant activity.

Ozen et al. synthesized twelve naphthalene-based conjugates and shows their anti-oxidant properties.

II. CONCLUSION

Recently demands of new drugs increases from novel organic compound naphthalene and its derivatives. These compounds possess various biological activities like anti-fungal, anti-bacterial, anti-oxidant, anti-inflammatory, anti-viral, cytotoxic activity etc. Naphthalene and their derivatives conjugates with different aryl compounds or heteroaryl compounds were examined and leads to discover new drugs, which very effective in pharmacological fields. Synthesized conjugates improved the bioactivity of the compound, which enhanced Lipophilicity of the resultant conjugate, this property improves the penetration power of conjugates into the targets and improves the drug-target interactions. The main aim of my work is the studies of naphthalene and their derived compounds in such a response to develop, design and identify potent drugs which curves many deadly diseases with little side effects.

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