



A REVIEW ON BIOLOGICAL ACTIVITIES OF INDOLE DERIVATIVES

Dr. Sudarshan Narayan Nagrale¹

Department of Pharmaceutical Chemistry
Dattakala College of Pharmacy, Swami Chincholi, Dist-Pune, Maharashtra, India.

Mr. Amit Vilas Pondkule²

Department of Pharmaceutics
Anusaya College of Pharmacy, Swami Chincholi, Dist-Pune, Maharashtra, India

Dr. Vishal Bharat Babar³

Department of Pharmaceutical Chemistry
Dattakala College of Pharmacy, Swami Chincholi, Dist-Pune, Maharashtra, India.

Mr. Vijay Sambhaji Sonavane⁴

Department of Pharmaceutics
Institute of Pharmaceutical Science and Research for Girls, Swami Chincholi, Dist-Pune, Maharashtra, India.

Abstract

Indole alkaloids are well characterized for various activities. Meanwhile, this situation scenario of disease depicting a different story, urge a call for novel scaffolds and pharmacophores. Indole scaffold has been found in several important synthetic drug molecules which gave a valuable idea for treatment and binds with high affinity to the multiple receptors helpful in developing new helpful derivatives.

Keywords: Antimicrobial activity, anticancer activity, Antibacterial Activity, Antifungal Activity.

Introduction

Indole, a planer heterocyclic molecule, widespread and in abundance in natural products also a part within the complex body part of many well-known medication. Therefore, indole derivatives have captured the eye of the scientific community because of their wide spectrum of biological activities, that embrace medicinal drug anti-tuberculosis, anti-tumor, anti-convulsion and anti-cardiovascular effects. Over the past few decades, many analysis teams and pharmaceutical corporations have according on vital medication molecules containing the indole moiety. These are applied for the treatment of acute or chronic inflammation also as a spread of inflammatory diseases. nonsteroidal anti-inflammatory drug may be a prospering anti-inflammatory drug drug (NSAID) in preventing sepsis and ALI, 30 and has led to the exploration of Tenidap a series of indole-based anti-inflammatory agents. Many of these candidates have been commonly used to reduce fever, pain, stiffness, and swelling by inhibiting the production of prostaglandins, as well as

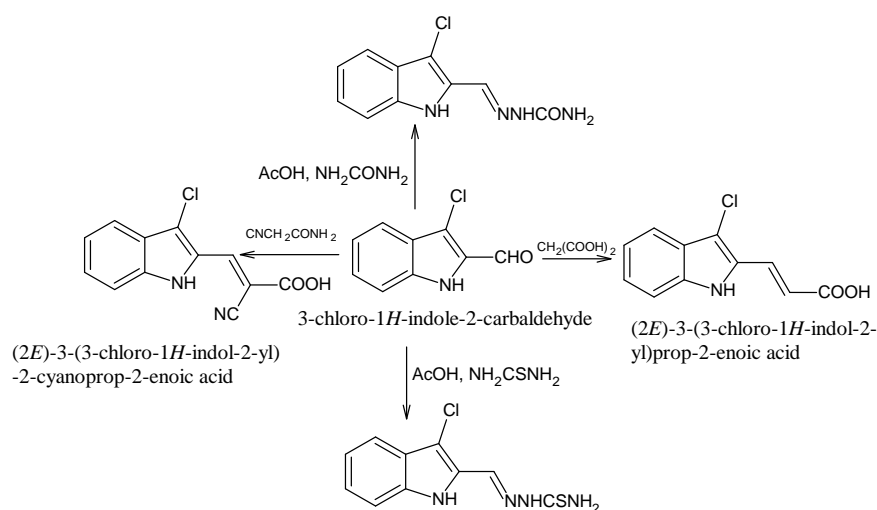
molecules known to cause these symptoms. However, to the simplest of our data, these medication are in the course of potential aspect effects, as well as headache, indigestion, heartburn, diarrhea, skin rash, or a sense of internal organ fullness.^[1]

The medicament activity of this category of compounds has been underexplored. Moreover, indole derivatives have fascinated importance in healthful chemistry, exhibiting medical specialty and therapeutic properties like antidepressant drug, antiplatelet, antihypertensive, herbicidal, and plant growth regulative properties. Indoles containing alternative heterocyclic moieties specially pyrazole and thiazole moieties have nice importance as inhibitor, antiproliferative, and antitumor agents within the gift work, we have a tendency to report on the economical synthesis of indole derivatives containing heterocyclic moieties like pyrazole, thiazole, and thiophen. This study centered on the synthesis and organic chemistry analysis of the new synthesized heterocyclic compounds that was then subjected through antimicrobial evaluations.^[2]

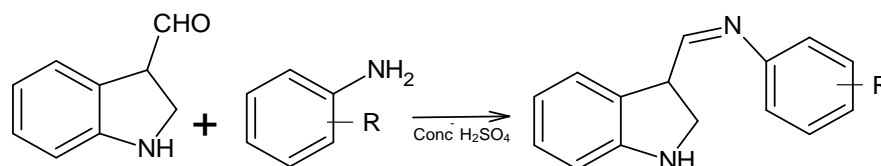
Different schemes for synthesis of Quinazolin-4(3H)-ones.

Indole nucleus is prevalent in numerous natural products and is extremely important in medicinal chemistry. The event of artificial ways resulting in indole derivatives has attracted a lot of attention in organic synthesis attributable to their biological activities.

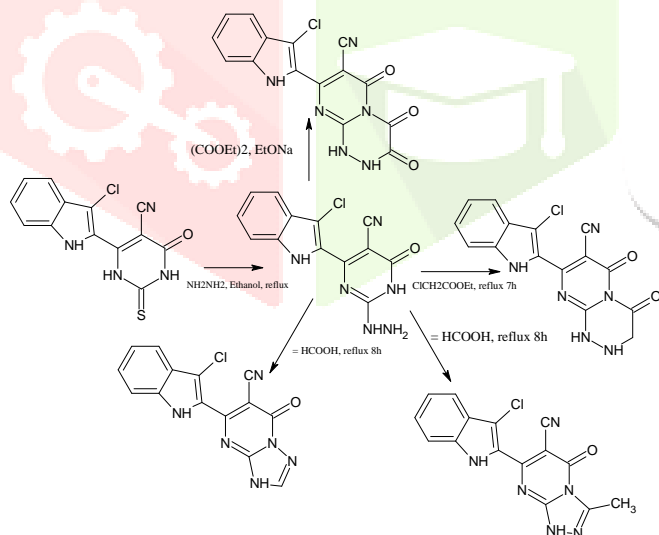
Mostafa Sayed. Et.al.2018. (Recently, indoles are considered fascinating heterocyclic compounds due to the fact of their big selection of organic activities such as antimicrobial activity. Herein, some new indole derivatives containing heterocyclic moieties were synthesized using 3-chloro-1H-Indole-2-carbaldehyde as a starting material, then allowed to react with compounds containing active methylene under Knoevenagel condensation and afforded the corresponding compounds. Also, the compound when allowed to react with hydrazine derivatives gave the corresponding thiosemicarbazone, semicarbazone, and hydrazone derivatives. All synthesized compounds had been evaluated for their antimicrobial activity. Compounds confirmed high antibacterial activity and compounds showed high antifungal activity.^[3]



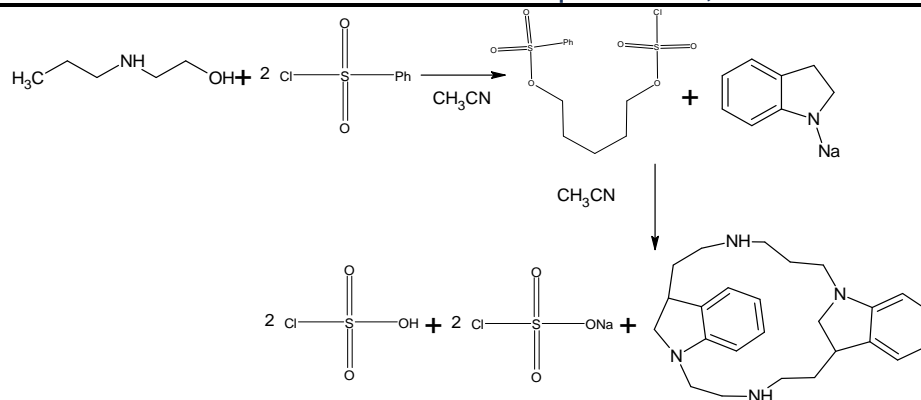
- 1) Imran Ali. Et.al. 2018 (Facile synthesis of micellar “nano” indole heterocyclic anti-cancer compounds are described. The synthesized compounds were characterised with the aid of UV-VIS, ^1H NMR, FT-IR and mass spectroscopy. The binding energies of DNA–compound adducts varies from 20.08 to 23.85 kJ mol $^{-1}$, and that they have been stabilised via hydrophobic interactions and H-bonding. The synthesized compounds enter into minor grooves of desoxyribonucleic acid throughout adduct formation..^[4]



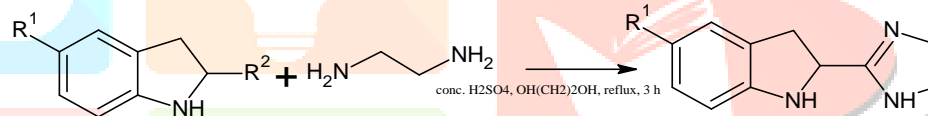
- 2) SAYED et. al. 2018 (Pyrimidines and pyrimidine bearing indole derivatives are very necessary species in chemistry due to the fact of their extensive use as bioactive compounds with a huge range of exceptional organic activities All compounds were screened for their in vitro antibacterial and antifungal activity, and they demonstrated promising results; all the new compounds synthesized from compound, which allowed reactions with thiourea and ethyl cyanoacetate, gave the target compound, which used to be used as a precursor for the synthesis of indolylthiazolopyrimidine derivatives by using reactions with halocarbonyl compounds such as chloroacetone, phencyl bromide, and chloroacetic acid through alkylation of the mercapto group followed by cyclization through a nucleophilic attack.^[5]



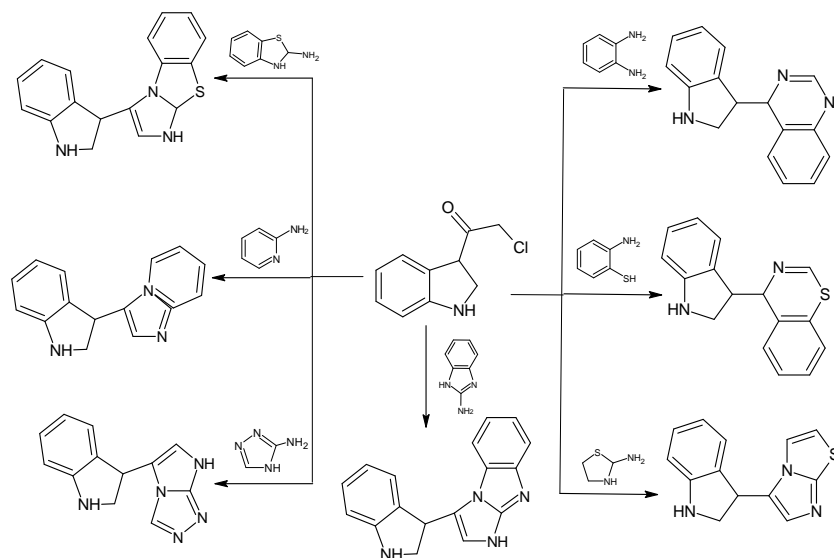
- 3) Fadhil B. Essa. Et.al. 2018 (Dibenzenesulphonyl diethyl amine has been prepared and used as a starting material to be introduced as an alkylating agent. Reaction of dibenzenesulphonyl diethyl amine with indole in the presence of sodium and absolute ethanol gave seven unexpected products, five of which were separated by flash chromatography. The antibacterial activity of compound 5 is very compatible with ampicillin.^[6]



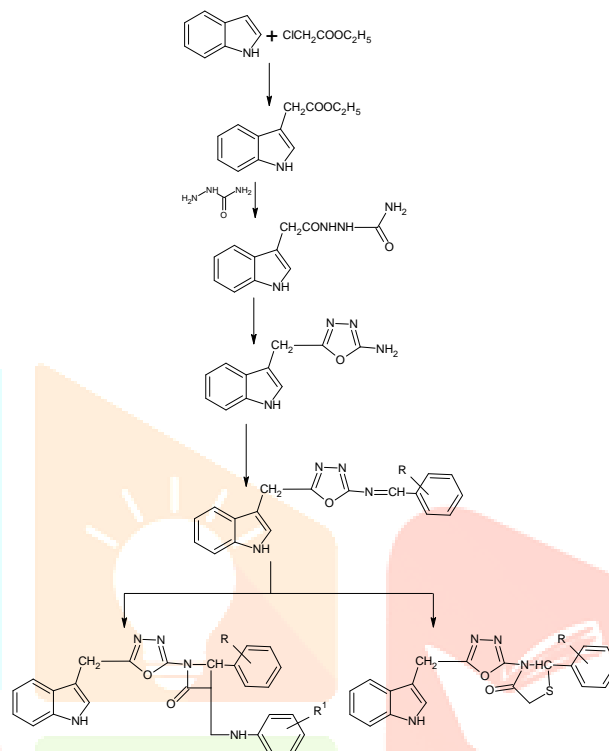
- 4) Humberto L. Mendoza-Figueroa. Et.al. 2018 (A series of 2- or 3-(4,5-dihydro-1H-imidazol-2-yl)-1H-indole derivatives were synthesized, characterized, and evaluated for their in vitro antibacterial and antifungal activities. Additionally, the synthesized compounds had been docked into the II DNA gyrase B active site, and their estimated binding modes have been inspected. Inhibitory activity was once tested in opposition to two species of Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*), two species of Gram-positive bacteria (*Staphylococcus aureus*, *Listeria monocytogenes*) and two fungi (*Candida albicans*, *Aspergillus niger*) the usage of the broth microdilution method. The docking effects anticipated that the imidazoline-indole hybrid moiety bind to the active site protein ATP-binding pocket from *E. coli* and *S. aureus* with good interaction energy scores. [7])



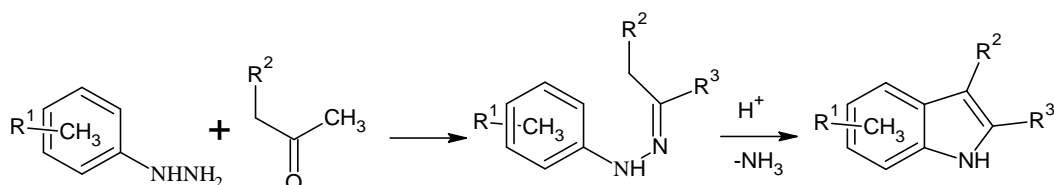
- 5) Ahmed El-Mekabaty. Et.al. 2018 (In a continuation of our program to boost a alternative class of antimicrobial and inhibitor agents, novel 3-substituted indole derivatives incorporating biologically lively heterocycles had been synthesized and evaluated for his or her in vitro antimicrobial activity.. Among the synthesized compounds, 3-(7H-imidazo[2,1-c] [1,2,4] triazol-5-yl)-1H-indole showed activity against *E. faecalis* equal to that of ampicillin and 50% greater endeavor than ampicillin towards *S. aureus* and *B. subtilis*. Also, 3-(7H-imidazo[2,1-c] [1,2,4] triazol-5-yl)- 1H-indole was discovered to exhibit strong in vitro antifungal recreation towards *Candida albicans*, *Aspergillus niger*, and *Penicillium sp.* [8])



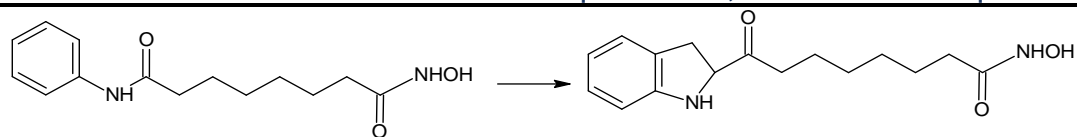
- 6) Archana. Et.al. 2018 (2-Amino-5-(3'-indolomethylene)-1, 3, 4 - oxadiazole undergoes facile condensation with various aromatic aldehydes to give 2-substituted arylidenylamino-5-(3'-indolomethylene) – 1, 3, 4 – oxadiazole The structures of these compounds have been hooked up on the foundation of analytical and spectral data. The newly synthesised compounds have been evaluated for their anticonvulsant activity and acute toxicity.^[9]



- 7) D.I.Bugaenko, A.V.Karchava, M.A.Yurovskaya. et.al. 2019 (Published records of the last 10 years regarding the development of new and upgrading of recognized strategies to indole synthesis are built-in and analyzed. Modern versions of the classical syntheses such as the Fischer synthesis, Nenitzescu synthesis, Ullmann reaction, Leimgruber ± Batcho synthesis, Reissert synthesis, Bartoli reaction, Madelung synthesis and Cadogan ± Sundberg reaction are considered. The new procedures consist of transformations of heterocycles, synthesis from o-alkynylanilines, reductive cyclization of nitrobenzene derivatives, synthesis with the use of arynes and catalysis by N-heterocyclic carbenes ^[10]

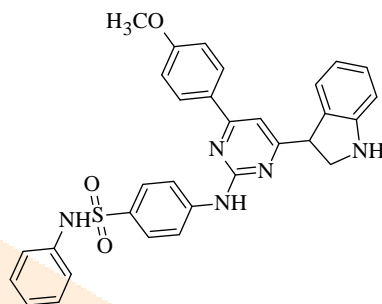


- 8) Sakineh Dadashpour. Et.al. 2018 (The indole scaffold is one in all the most important big heterocycles within the current and artificial bioactive compounds as nicely as antitumor agents. due to the fact of its diversity and flexibility, it's been an extraordinarily privileged motif for the target-based style and development of antitumor agents. inside the last decade, various researchers have according varied indole-based compounds with distinct mechanisms concerned in manufacturing achievable antitumor activities, indicating the importance of indole motif within the antitumor drug development ^[11]

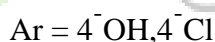
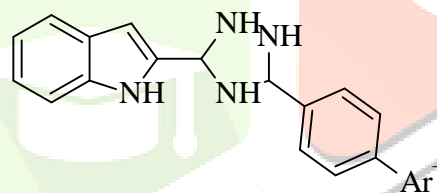


ANTIMICROBIAL ACTIVITY:-

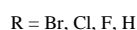
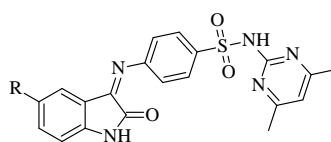
Nassar et al, Synthesis (in vitro) Antitumor and antimicrobial activity of some pyrazoline, pyridine and pyrimidine derivative linked to indole moiety. The anti-bactericidal undertaking against Gram tremendous bacteria *Staphylococcus aureus* and Gram-negative micro organism *Escherichia Coli* and *Pseudomonas aeruginosa* [12]



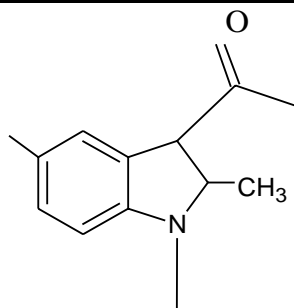
Banu et al, de novo drug design and synthesis of certain indole derivative and screening for their xanthenes oxides inhibitory activity. The synthesis compound was screening for their xanthenes oxides inhibitory activity. The synthesis compound was once screened for their in vitro antibacterial exercise against *Escherichia coli* and *Pseudomonas aeruginosa* [13]



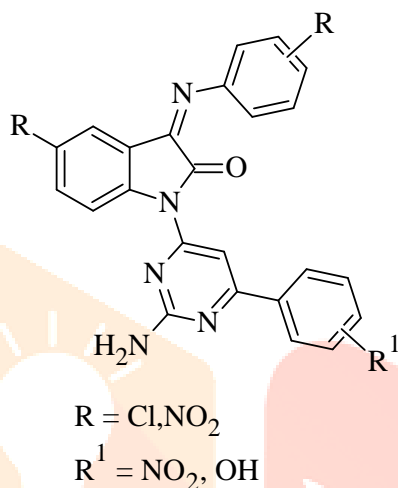
Selvam et al, anti-influenza virus activities of 4-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene) amino]-N-(4,6-dimethyl-2-pyrimidin-2-yl) benzenesulphonamide and its derivative. The antimicrobial recreation towards *E.coli*, *S.aureus*, *P.aeruginosa*, *B.subtilis* [14]



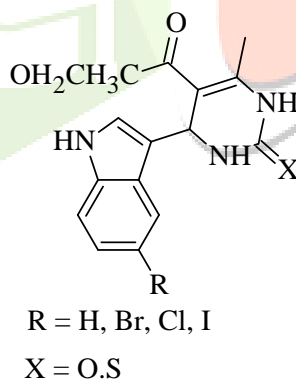
Bhovi et al, Chemoselective reaction of indole 1,3-dicarboxylates closer to hydrazine hydrate bisheterocycles: Synthesis and antimicrobial exercise of some new-2-methyl-3-ethoxycarbonyl-1-oxadiazolyl / thiazolidinonyl / pyrrolyl-aminocarbonylmethylindoles. [15]



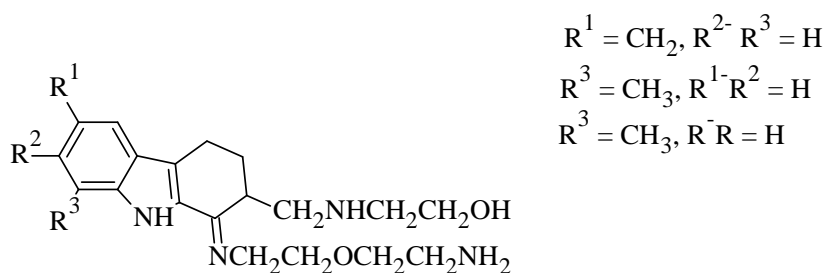
Mondal et al, Synthesis of novel mercapto-pyrimidine and amino-pyrimidine derivatives of indoline-2-one as attainable antioxidant and antibacterial agent. The synthesis compounds have been screened for their in vitro antibacterial activity towards *Escherichia coli* and *Pseudomonas aeruginosa*. [16]



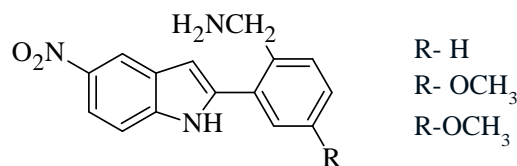
Heda et al, is that the investigated Synthesis and antimicrobial recreation some derivatives of 5-substituted indole dihydropyrimidines. The synthesis compounds were screened for their in vitro antibacterial activity against *Escherichia coli* and *Pseudomonas aeruginosa*. [17]



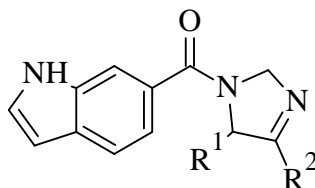
Martin et al, synthesis and characterization of carbazole derivatives and their antimicrobial studies. The antimicrobial recreation against *E.coli*, *S.aureus*, *P.aeruginosa*, *B.subtilis*. [18]



Samosorn et al, Synthesis of functionalized 2-aryl-5-nitro-1H indole and their activity as antibacterial The action of the antibacterial agent barbering by using blocking the NorA MDR pump in S.aureus. [19]

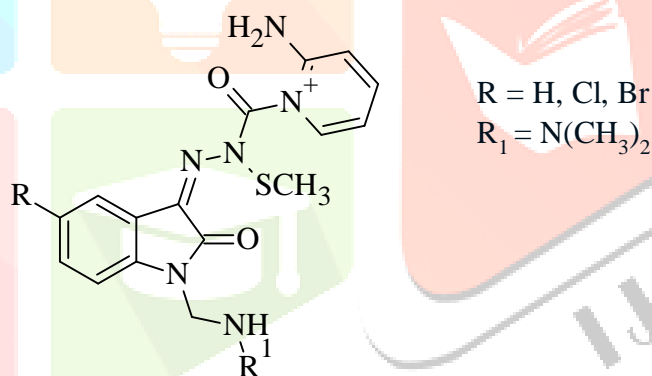


Sarma et al, A facial Synthesis and antimicrobial activity of some pyrazole derivatives carrying indole. All the newly synthesized compounds are by elemental evaluation and spectral studies and evaluated for antimicrobial activities. [20]



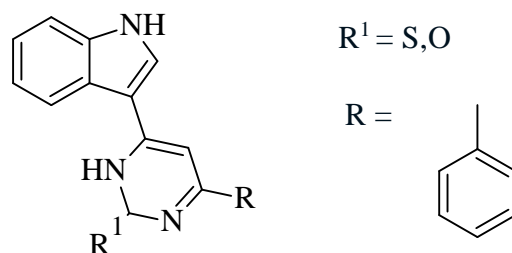
Antimicrobial and Anti-HIV Activities:-

Pandeya et al, is studied the synthesis, antibacterial, antifungal and anti- HIV comparison of Schiff bases of isatin derivatives with 3-amino-2-methylmercapto methylmercaptoquinazolin- 4(3H)-one. [21]

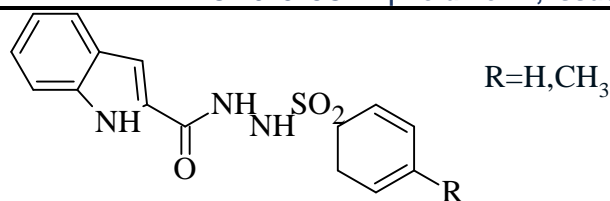


Anti-Inflammatory and Analgesic Activity:-

Amir et al, Synthesis and biological comparison of some 4-(1H-indol-3-yl)-6-phenyl-1,2,3,4-tetrahydropyrimidin-2-ones / thiones as amazing medicinal drug agents. medicinal drug activity whereas the quality drug ibuprofen is employed. [22]

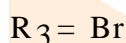
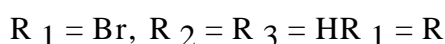
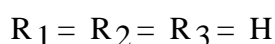
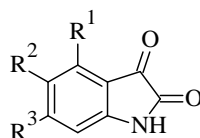


Sondhi et al, microwave power assisted synthesis of indole and furan derivatives possessing best anti-inflammatory and analgesic activity. The synthesized compound has been screened for anti-inflammatory and analgesic activity. [23]



Anticancer Activity: -

Kara et al, is studied the invitro cytotoxicity analysis of some substituted isatin derivatives. All synthesized compound is screened by antitumor activity. [24]



Conclusion

Indole derivatives are very vital heterocyclic compounds in the drug-discovery studies. The reviewed indole moiety has proven a broad spectrum of biological activities. These scaffolds bind without problems to a multitude of receptors and therefore their synthesis represents a promising way for new lead compounds.

The indole nucleus-based pharmaceutical are unexpectedly turning into very essential class of therapeutic agents and are likely to replace many existing organic based pharmaceuticals in the very near future. There has been an growing activity in the use of indole derivatives as amazing molecules in opposition to cancer cells, Microorganism and a variety of kinds of diseases.

References

- 1) Nagendra K, Neha K and Eun Ha Choi. Biomedical importance of Indoles. 2013;18(6):6620-6682.
- 2) Mostafa Sayed, Adel M, Mostafa A and Reda H. synthesis of some heterocyclic compounds derived from indole as antimicrobial agents. 2018(1):1532-2432.
- 3) Sayed M, Kamal El-Dean AM, Ahmed M, Hassanien R. Synthesis of some heterocyclic compounds derived from indole as antimicrobial agents. Synthetic Communications. 2018 Feb 16;48(4):413-21.
- 4) Ali I, Mukhtar SD, Hsieh MF, Allothman ZA, Alwarthan A. Facile synthesis of indole heterocyclic compounds based micellar nano anti-cancer drugs. RSC advances. 2018;8(66):37905-14.
- 5) Sayed M, Kamal El-Dean AM, Ahmed M, Hassanien R. Design, synthesis, and characterization of novel pyrimidines bearing indole as antimicrobial agents. Journal of the Chinese Chemical Society. 2019 Feb;66(2):218-25.
- 6) Essa FB, Bazbouz A, Alhilal S, Ouf SA, Gomha SM. Synthesis and biological evaluation of an indole core-based derivative with potent antimicrobial activity. Research on Chemical Intermediates. 2018 Sep;44(9):5345-56.

- 7) Mendoza-Figueroa HL, Serrano-Alva MT, Aparicio-Ozores G, Martínez-Gudiño G, Suárez-Castillo OR, Pérez-Rojas NA, Morales-Ríos MS. Synthesis, antimicrobial activity, and molecular docking study of fluorine-substituted indole-based imidazolines. *Medicinal Chemistry Research*. 2018 Jun;27(6):1624-33.
- 8) El-Mekabaty A, El-Shora HM. Synthesis and evaluation of some novel 3-hetarylindole derivatives as antimicrobial and antioxidant agents. *Chemistry of Heterocyclic Compounds*. 2018 Jun;54(6):618-24.
- 9) Archana SS. Synthesis and Anticonvulsant Studies of Thiazolidinone and Azetidinone Derivatives from Indole Moiety.
- 10) Bugaenko DI, Karchava AV, Yurovskaya MA. Synthesis of indoles: recent advances. *Russian Chemical Reviews*. 2019 Feb 1;88(2):99.
- 11) Dadashpour S, Emami S. Indole in the target-based design of anticancer agents: A versatile scaffold with diverse mechanisms. *European journal of medicinal chemistry*. 2018 Apr 25; 150:9-29.
- 12) Nassar E. Synthesis (in vitro) Antitumor and antimicrobial activity and pyrimidine derivatives linked to indole moiety. *J American sci*2010;6(8):463-471.
- 13) Banu s, Manjula A, Lath Mary T, Ravi T. De Nova drug design and synthesis of certain indole derivatives and screening for their xanthine oxidase inhibitory activity. *Int J Pharm Tech Res* 2010;2(4):2128-2138.
- 14) Selvam P, Murgesh N. Anti-influenza virus activities of 4-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)amino]-N-(4,6-dimethyl-2-pyrimidin-2-yl) benzenesulphonamide and its derivatives. *Int Medical Press* 2006;17:269-274.
- 15) Bhavi M, Gadaginamath G. Chemoselective reaction of indole 1,3-dicarboxylates towards hydrazine hydrate bisheterocycles: Synthesis and antimicrobial activity of some new-2-methyl-3-ethoxycarbonyl-1-oxadiazolyl / thiazolidinonyl / pyrrolyl-aminocarbonylmethylindoles. *Indian J Chem* 2005;44B:1663-1668.
- 16) Mondal P, Jana S. Synthesis of novel mercaptopyrimidine and amino-pyrimidine derivatives of indoline -2-one as potential antioxidant and antibacterial agent. *Pharm Res* 2010;3:17-26.
- 17) Heda L, Sharma R, Pareek C. Synthesis and antimicrobial activity of some derivatives of 5-substituted indole dihydropyrimidines. *E-J Chem*. 2009;3(6):770-774.
- 18) Martin A, Karnam R. Synthesis and characterization of carbazole derivatives and their antimicrobial studies. *Acta Pharm* 2006;56:79-86.
- 19) Samosorn S, Bremner J, Ball A. Synthesis of functionallised 2-aryl-5-nitro-1H-indoles their activity as bacterial NorA efflux pump inhibition. *Bioorganic Med Chem*2006;14:857-865.
- 20) Sarma N, Subha M, Rao K. A facial Synthesis and antimicrobial activity of some pyrazole derivatives carrying indole. *E-J Chem* 2010;7(3):745-750.
- 21) Pandeya SN, Sriram D, Nath G. Synthesis, antibacterial, antifungal and anti-HIV evaluation of Schiff and Mannich bases of isatin derivatives with 3-amino-2-methylmercaptoquinazolin-4(3H)-one. *Pharmaceutica Acta Helvetiae* 1999;74:11-7.
- 22) Amir M, Javed S, Kumar H. Synthesis and biological evaluation of some 4-(1H-indol-3-yl)-

6-phenyl-1,2,3,4-tetrahydropyrimidin-2-ones / thiones as potent anti-inflammatory agents.

Acta Pharm 2008;58:467-477.

23) Sondhi SM, Jain S, Rani R, Kumar A. Microwave assisted synthesis of indole and furan derivatives possessing good anti-inflammatory and analgesic activity. Indian J Chem 2007;46B:1848-1854.

24) Kara L, Vine, Julie M, Locke, Marie R. In vitro cytotoxicity evaluation of some substituted isatin derivatives. Bioorganic and Medicinal Chemistry 2007;15:931-8.

