



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**<http://doi.org/10.5281/zenodo.1206386>Available online at: <http://www.iajps.com>

Review Article

**INDOLES AS THERAPEUTICS OF INTEREST IN MEDICINAL
CHEMISTRY**C. Buvana^{1*}, R. Suresh¹, Y. Haribabu², P. K. Manna¹^{1*},²Department of Pharmaceutical chemistry, Grace College of Pharmacy, Palakkad, Kerala.¹Department of Pharmacy, Faculty of Engineering and Technology, Annamalai University, Chidambaram, Tamilnadu, India**Abstract:**

Indole is a valuable compound which has become prominent in medicinal chemistry because of its various biological activities. Indole ring is present in various marine or terrestrial natural compounds, which have useful biological properties. In last few years it was reported that indole, its bioisosters and derivatives had antimicrobial activity against gram-negative, gram-positive bacteria and yeast candida albicans antimicrobial activity. A large number of efforts were made to synthesize different heterocyclic compounds and their derivatives in the past decade and were found to possess promising antitumor, anticonvulsant, antimicrobial anti-tubercular and anti-diabetic activities. Although indole moiety is very small but is fascinated by scientists because of the diverse biological activities by not only indole but its various substituted derivatives as well. This review is focused on the indole and its derivatives that are now in development. This review brings about an overview of novel drug molecules of indole and also urges to synthesize more moieties for better enhanced biological activity.

Keywords: *Indole, Antimalarial, Anticancer, Antimicrobial, Antihypertensive***Corresponding author:**

C. Buvana,
Department of Pharmaceutical Chemistry,
Grace College of Pharmacy,
Palakkad,
Kerala.
E-mail: boviblue@gmail.com

QR code



Please cite this article in press C. Buvana et al., *Indoles as Therapeutics of Interest in Medicinal Chemistry*, *Indo Am. J. P. Sci*, 2018; 05(03).

INTRODUCTION: [1]

The name *indoleis* portmanteau of the words *indigo* and *oleum*. Indole is an aromatic heterocyclic organic compound. It has a bicyclic structure, consisting of a benzene ring and a pyrrole nucleus are fused in 2, 3 positions of the pyrrole ring. Indole is non-basic nitrogenous compound. 1-3 Indole chemistry began to develop with the study of the dye indigo. The word Indole is coined from the word India, a blue dye imported from India known as Indigo. Indigo can be converted to isatin and then to oxindole. 4-5 In 1866, Adolf von Baeyer reduced oxindole to indole[1] by using zinc dust. In 1869; he proposed a formula for indole.

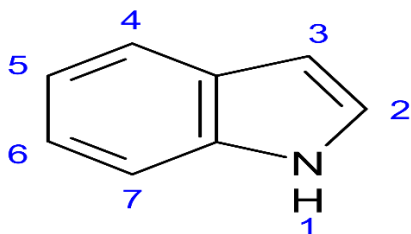


Fig. 1: Bayer's structure of indole

Indole derivatives occur widely in natural products, plants, animals and marine organisms.¹⁶ Many

natural products contain indole nucleus like heteroauxin[2], tryptophan [3], hypaphorine[4], bufotenin[5] and gramine[6] [Fig. 1]. Various plants contain indole as a core component like *Robiniapseudacacia*, Jasmine, citrus fruits and orange blossoms. Serotonin [7] contains indole nucleus and is biochemically derived from tryptophan, is a neurotransmitter and is found in all bilateral animals. Melatonin [8], is a hormone found in animals, plants, and microbes and meant for the control of diurnal rhythm of physiological functions. An indole alkaloid like Ajmaline [9], Reserpine [10] is used to treat high blood pressure and severe agitation in patients with mental disorders. Vinblastine is anticancer agent being recognized tubulin polymerization inhibitor and used in the treatment of acute lymphoblastic leukemia and against both Hodgkins and non-Hodgkin's lymphoma. Sumatriptan [11] and ondansetron [12] are highly selective medicines for the treatment of migraine and suppression of nausea, vomiting caused by cancer chemotherapy respectively. Indomethacin [13] is a non-steroidal anti-inflammatory drug commonly used to reduce fever, pain, stiffness and swelling by inhibiting production of prostaglandin [2-12].

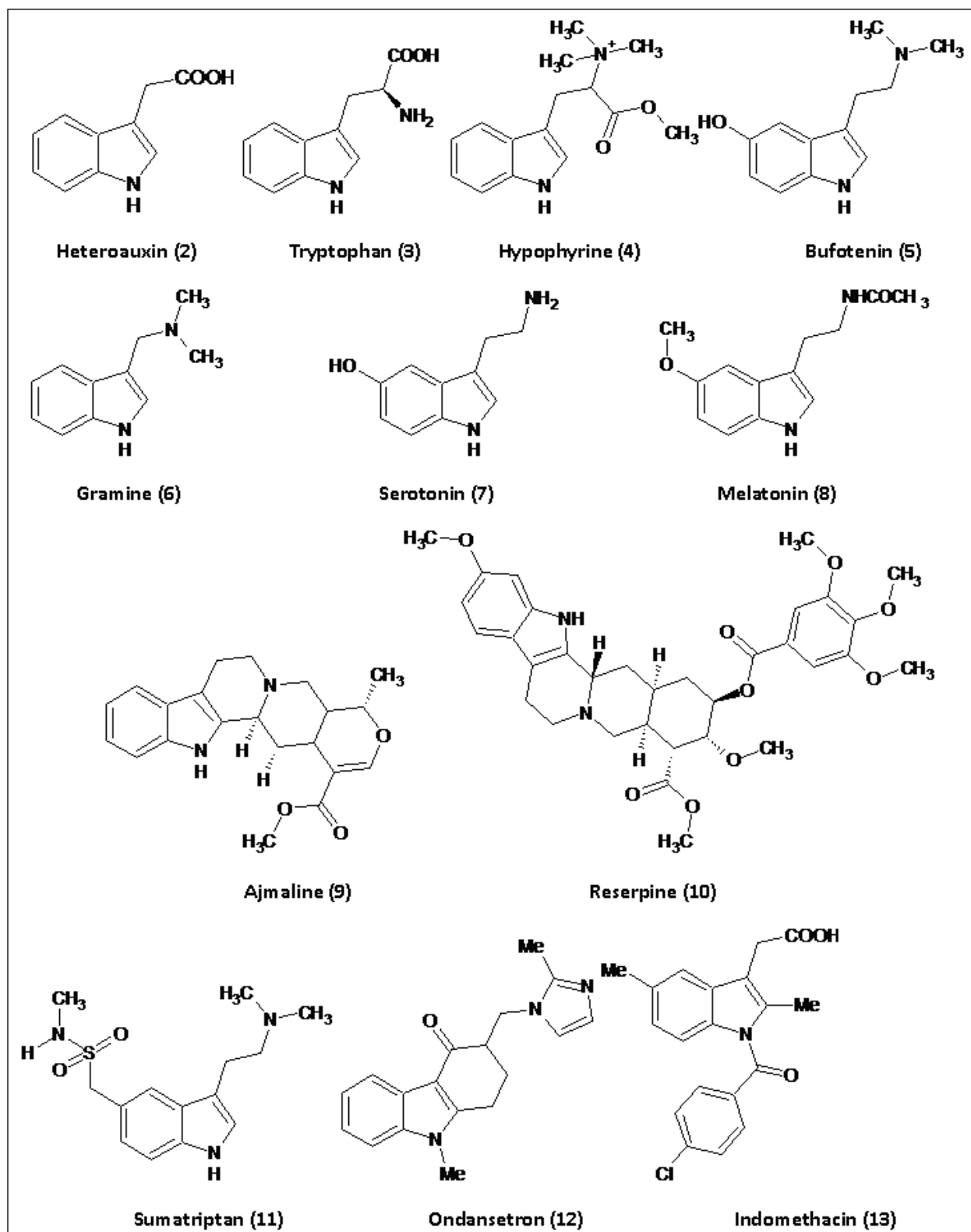


Fig. 2: Structures of indole containing natural products and drugs

Indole represents one of the most important structural motifs in drug discovery, and it is described as one of the "privileged scaffolds". Indole derivatives and its

pharmacological significance provides tremendous opportunities to discover novel drugs with different modes of action.

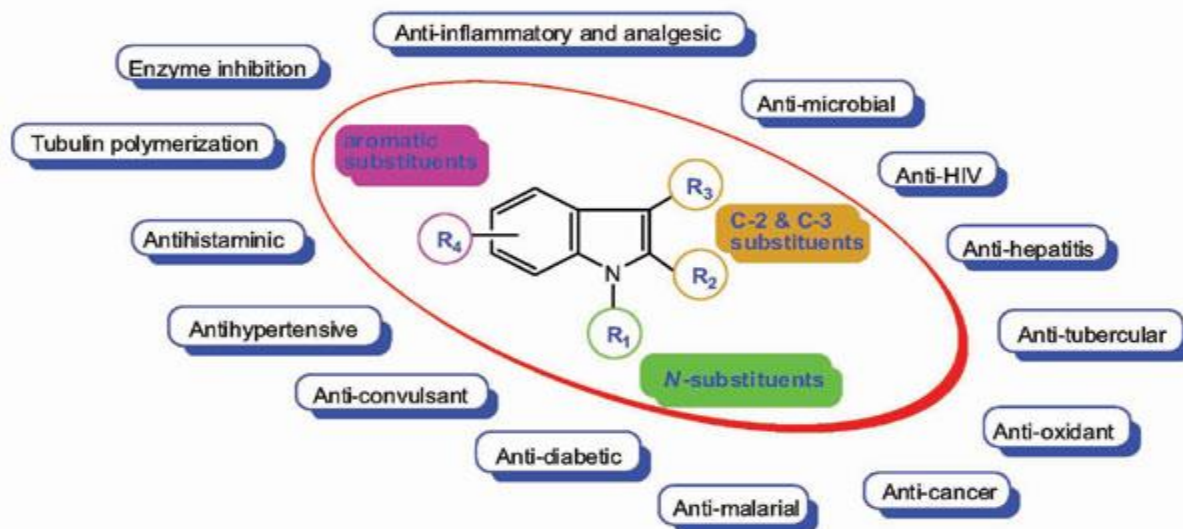
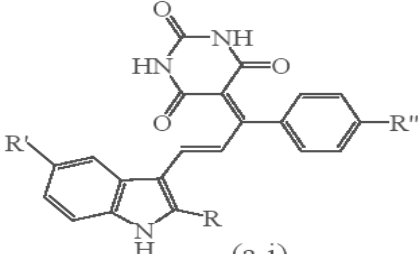
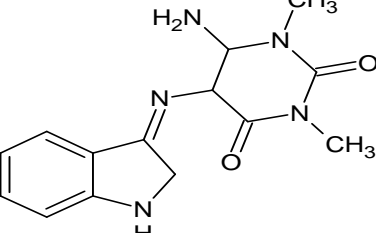
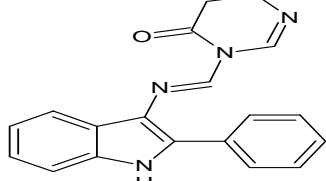
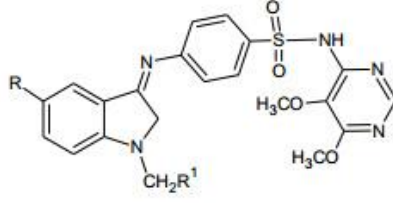
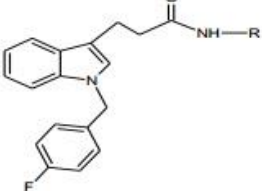
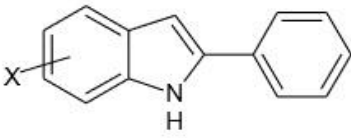
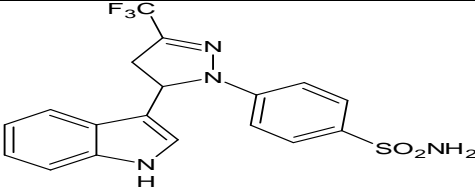
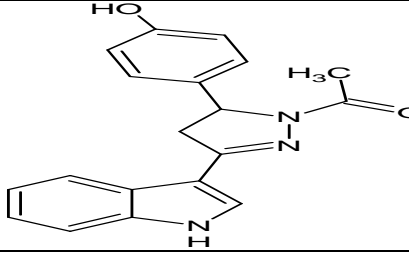
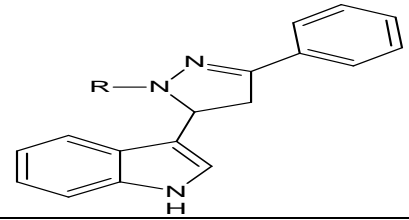
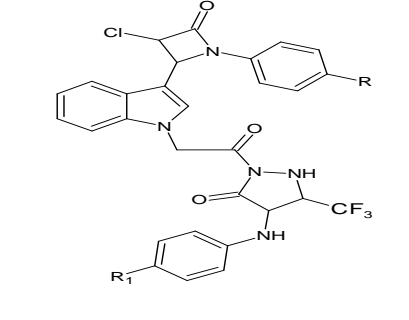
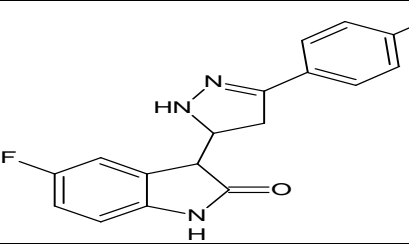
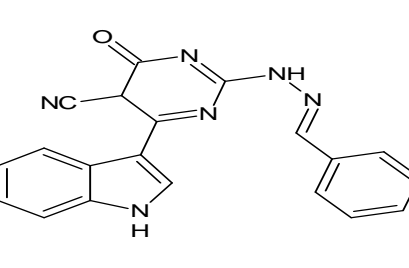
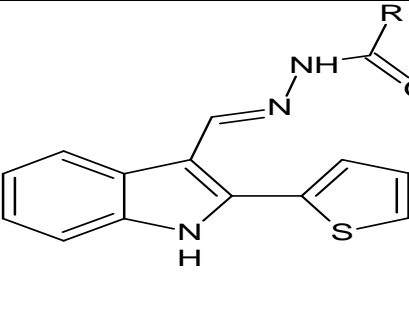
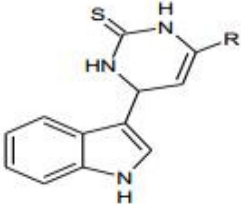
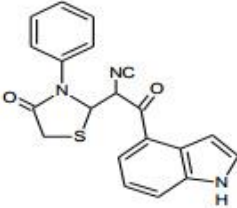
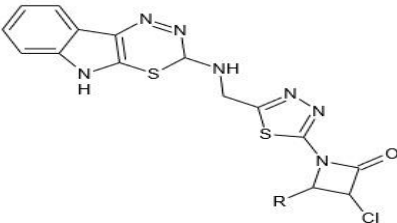
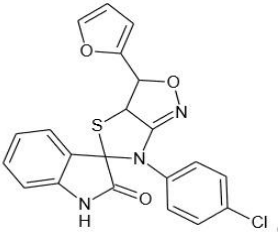
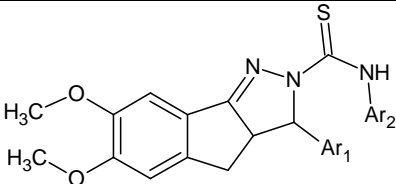
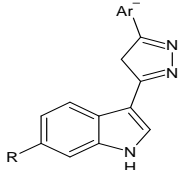
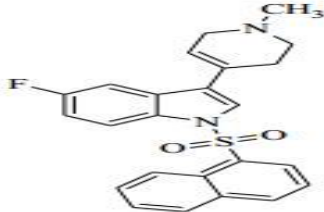


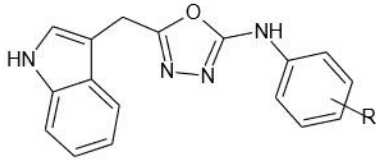
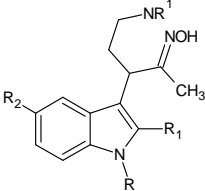
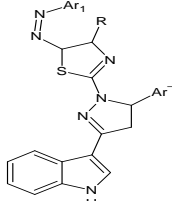
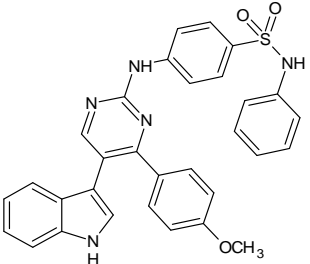
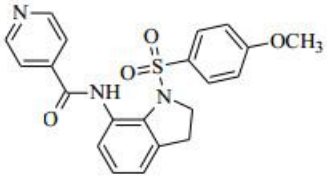
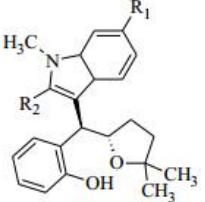
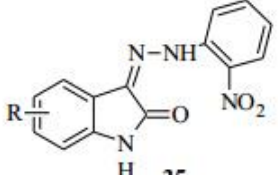
Fig. 3: Pharmacological significance of indole

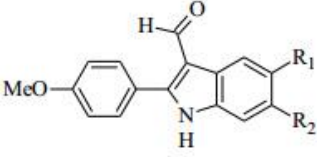
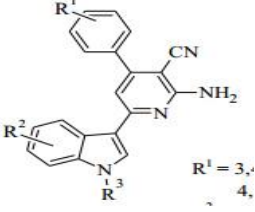
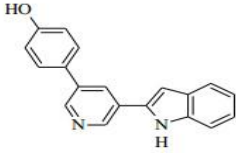
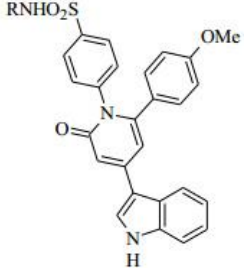
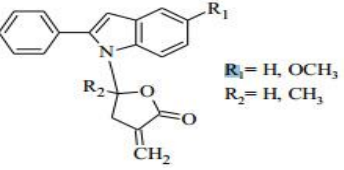
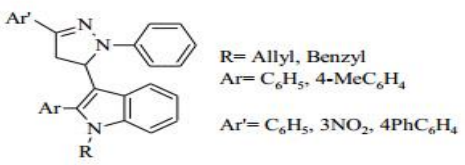
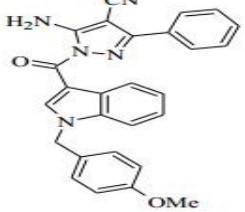
AUTHOR	SYNTHESISED COMPOUNDS	THERAPEUTIC INDICATION
<p>Antimicrobial activity Heba m. abo-salem et al [13]</p>		Antimicrobial activity
<p>Adel hamed mandour et.al[14]</p>		Antimicrobial activity
<p>Mari'a C. et al[15]</p>		Antimicrobial activity
<p>Faritha A et al [16]</p>		Antimicrobial activity

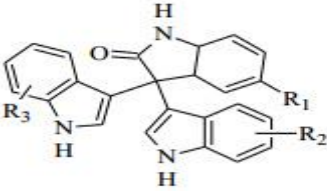
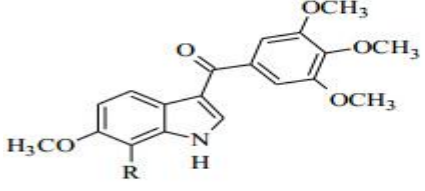
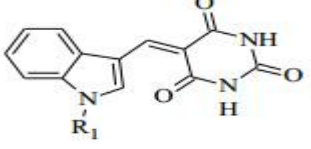
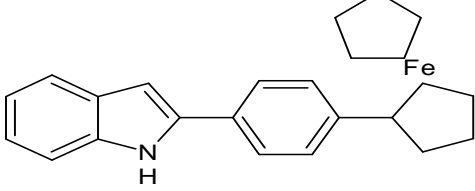
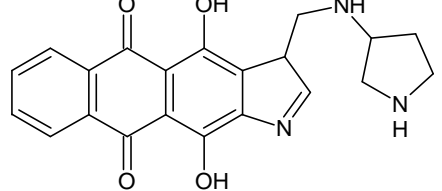
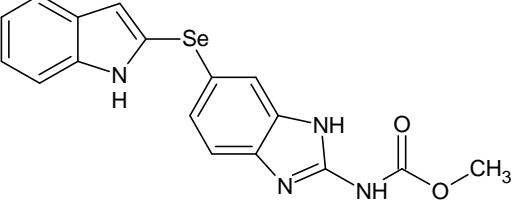
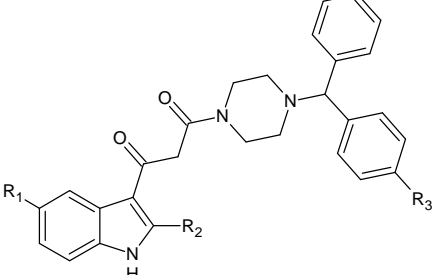
<p>Jaiprakash S. Biradar et al., [17]</p>	 <p>(a-i)</p>	<p>Antimicrobial agents.</p>
<p>Saundane Anand R et.al., [18]</p>		<p>Antimicrobial Activity</p>
<p>Asmaa S et.al[19]</p>		<p>Antimicrobial Activity</p>
<p>Pandeya S.N. et.al[20]</p>		<p>Anti microbial agent</p>
<p>SüreyyaÖlgena,Nurt en Altanlarb et. al. [21]</p>	 <p>R= 4-Cl-phenyl, 4-F-phenyl, 2,4-Cl-phenyl</p>	<p>Antimicrobial, antifungal and anti-HBV activities</p>
<p>Kumar et al[22]</p>		<p>Antibacterial and anti-inflammatory activit</p>
<p><u>Antiinflammatory activity</u> Reddy et al[23]</p>		<p>Anti-inflammatoryactivity</p>

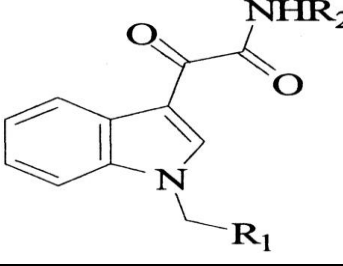
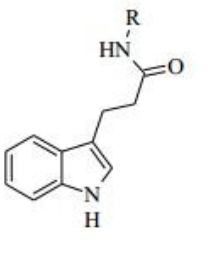
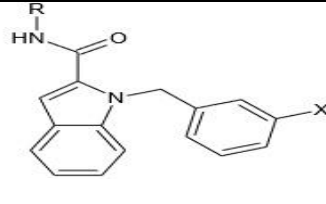
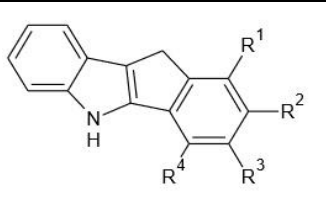
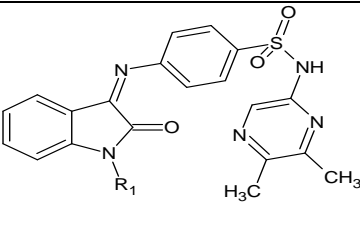
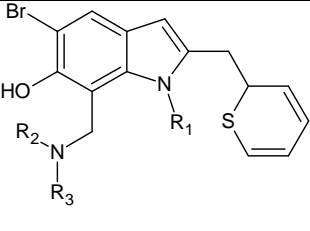
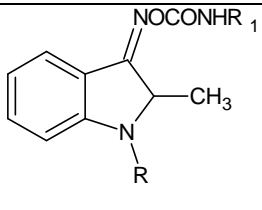
Rani et al[24]		Anti-inflammatory
Minakshi Shroff et al[25]		Anti-inflammatory
SMuralikrishna et al[26]		Anti-inflammatory activity
El-Sayed et al. [27]		Cyclooxygenase [COX] inhibition
Mohammad mumtaz alam et al., [28]		Anti-inflammatory and antimicrobial activity
Sally et al [29]		Antitumor and Anti-inflammatory

Amir et.al[30]		Anti-inflammatory agents
Radwanet.al[31]		Analgesic activity
Kumar et al[32]		Anti-inflammatory activity
Manaet al[33]		Anti-inflammatory activity
<u>Anticonvulsant & anti depressant activity</u> Mohamed Jawed Ahsan, et al[34]		Anticonvulsant activity
Pravin O patil et al[35]		Antidepressant and anticonvulsant
Slasi,A et. al[36]		Treatment of CNS disease

Siddiquet al[37]		Anticonvulsant
Abele et al. [38]		Antidepressant activity
Anti-cancer activity Abdou O. et al[39]		Anticancer Agents
Asmafahmy et al[40]		Anti tumour&anti microbial activity
Liou et al[41]		Anticancer agents
Sigman et al[42]		Anticancer activity against MCF-7 cells
Popp and Pajouhesh et al[43]		Lymphoid leukaemia

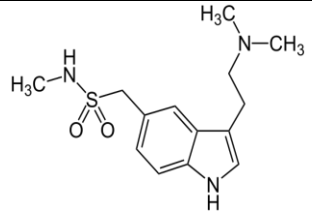
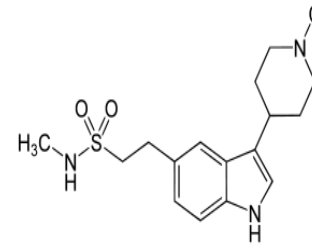
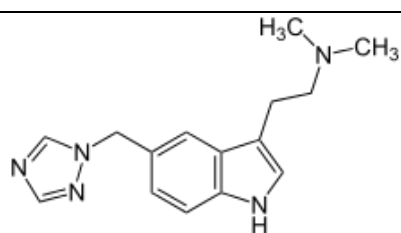
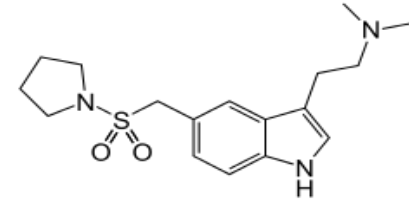
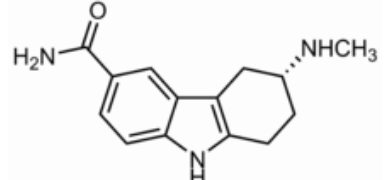
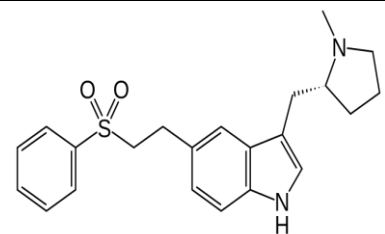
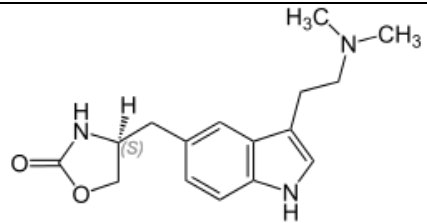
Doris Kaufmann et al[44]		Treatment of breast cancer
Fan Zhang et al[45]	 <p>$R^1 = 3,4$ $R^2 = 4$</p>	Anti-tumor activity
Ulrich Jacquemard et al[46]		CDK inhibitors and cytotoxic agents
Ekhl Nassar et al[47]		Antitumor and antimicrobial activity
Huasheng Ding et al[48]	 <p>$R_1 = H, OCH_3$ $R_2 = H, CH_3$</p>	Potent inhibitors for AKT-m TOR signaling pathway kinases
Magdy A H Zahran et al[49]	 <p>$R = \text{Allyl, Benzyl}$ $Ar = C_6H_5, 4-MeC_6H_4$ $Ar' = C_6H_5, 3NO_2, 4PhC_6H_4$</p>	Antitumor activity
Abdel-Rahman Farghaly et al[50]		Antitumor activity

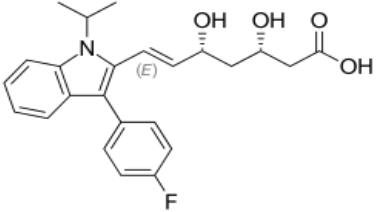
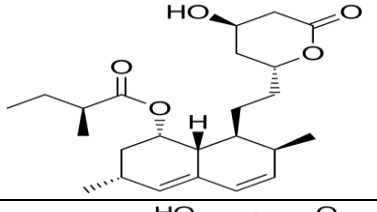
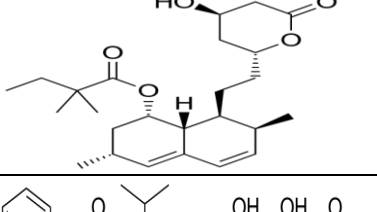
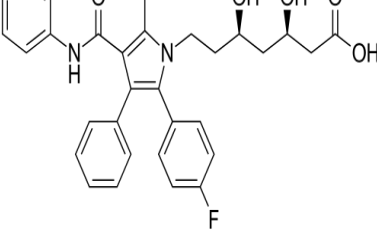
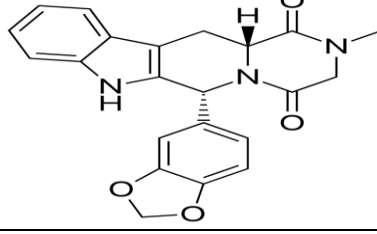
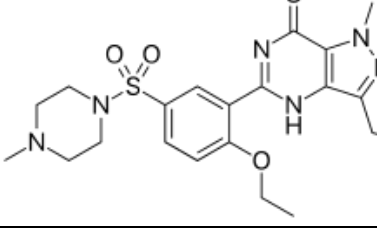
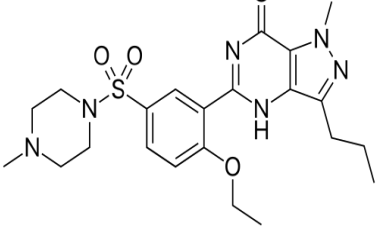
Ahmed Kamal et al[51]	 <p> $R_1 = \text{H, 5Cl, 5Br, 5NO}_2$ $R_2 = \text{H, F}$ $R_3 = \text{H, CH}_3$ </p>	Anticancer activities
Yu-Shan Wu et al[52]	 <p>$R = \text{I, CH}_3, \text{CH}_2\text{CH}_3$</p>	Anticancer activities
Palwinder Singh et al[53]	 <p> $R_1 = \text{H, butene, butyne, C}_6\text{H}_5, \text{ethane, C}_6\text{H}_5\text{COCH}_3, \text{ClC}_6\text{H}_4\text{COCH}_3$ </p>	Anticancer activities
Radulovicet al[54]		Anticancer agents.
Shchekotikhinet al[55]		Anticancer agents.
Guan et al[56]		Anticancer agents.
Jun-Rong Jiang et al[57]		Anticancer activity

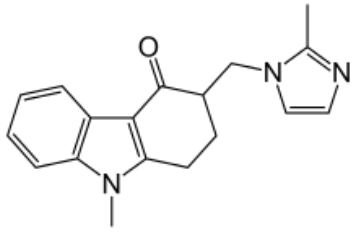
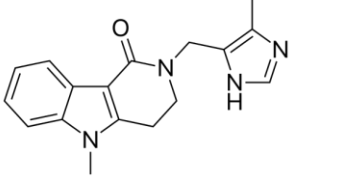
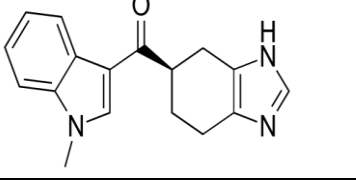
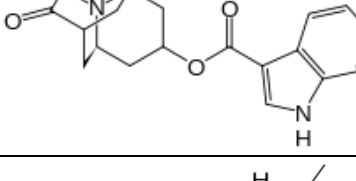
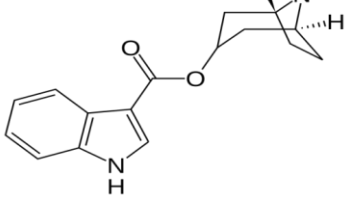
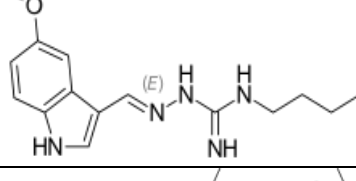
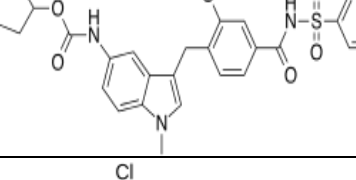
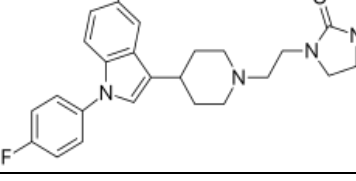
Wen-Tai Li <i>et al</i> [58]		Orally Anticancer activity
<u>ANTIOXIDANT PROPERTY</u> Zeynepates-alagoz <i>et. Al</i> [59]		Antioxidant property
Enienet <i>al</i> [60]		Antioxidant property
Talazet <i>al</i> [61]		Antioxidant property
<u>ANTIVIRAL ACTIVITY</u> Selvamet <i>al</i> [62]		Antiviral activity
Dun Wang <i>et al</i> [63]		Antiviral activity
Abele <i>et al.</i> [64]		Antiviral activity

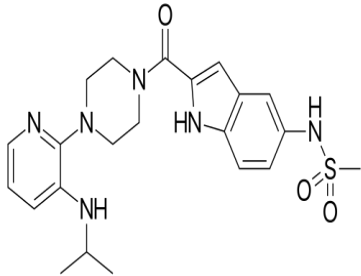
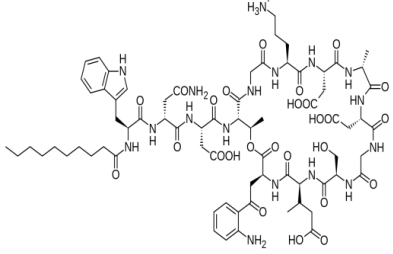
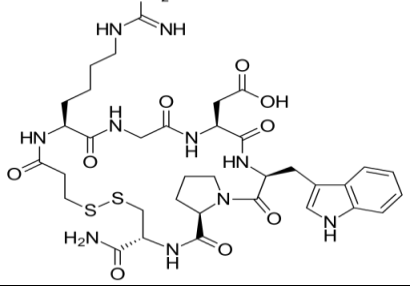
There are also an amazing number of indole containing drugs in the market.

INDOLE-CONTAINING DRUGS[65]

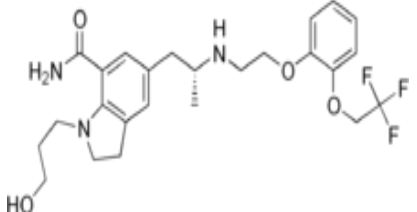
NAME OF THE DRUG	STRUCTURE	COMPANY NAME	BRAND NAME	THERAPEUTIC APPLICATION
1. Triptans a) Sumatriptan		Glaxo smithkline	Imitrex	Antimigraine
b) Naratriptan		Glaxosmithkline	Naramig	Antimigraine
c) Rizatriptan		Merck	Maxalt	Antimigraine
d) Amlotriptan			Axert	Antimigraine
e) Frovatriptan		Glaxosmithkline	Frova	Antimigraine
f) Eletriptan		Pfizer	Relpax	Antimigraine
g) Zolmitriptan		Glaxosmithkline	Zomig	Antimigraine

2. a) Fluvastatin		Merck	Lescol, Lescol XL	Treatment of Hypercholesterolemia & lipoproteinemia
b) Lovastatin		Novartis	Mevacor, Altoprev, Altacor	Treatment of Hypercholesterolemia & lipoproteinemia
c) Simvastatin		Novartis	Zocor, FloLipid	Treatment of Hypercholesterolemia & lipoproteinemia
d) Atrovastatin		Pfizer	Lipitor	Treatment of Hypercholesterolemia & lipoproteinemia
3. a) Tadalafil		Apollo Life Sciences Pvt Ltd	Adcirca, Cialis	Used to treat erectile dysfunction or pulmonary arterial hypertension;
B) Sildenafil		Pfizer	Revatio, Viagra	used to treat erectile dysfunction and pulmonary arterial hypertension
c) Vardenafil		A.D.Pharmaceuticals	Levitra.	used for treating erectile dysfunction

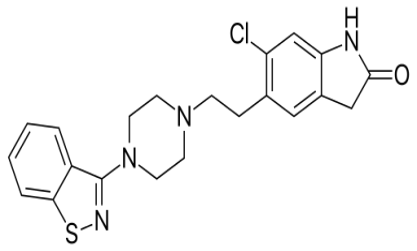
4. a) Ondansetron		Glaxosmithkline	Zofran	Antiemetic caused by cancer chemotherapy, radiation therapy, or surgery
b) Alosetron		Glaxosmithkline	Lotronex	Antiemetic
c) Romosetron		AstellasPharma	Nozia	Antiemetic
d) Dolasetron		Sanofi- Aventis	Anzemet	Antiemetic
e) Tropisetron		Astamedica	Novoban	Antiemetic
5. Tegaserod		Novartis	Zelmac	Totreat chronic idiopathic constipation
6. Zafirlukast		Astra Zeneca	Accolate	used for the chronic treatment of asthma
7. Sertindole		Lundbeck	Compazine	antipsychotics,

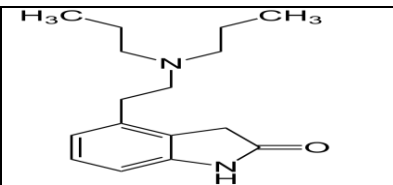
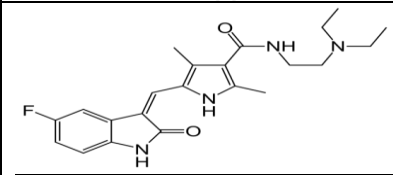
8. Delavirdine		Pfizer	Rescriptor	Highly active antiretroviral therapy [HAART] for the treatment of [HIV] type 1
9. Daptomycin		Lilly/cubist	Cubicin	antibiotic
10. Eptifibatid		COR Therapeutics/ schering-plough	Integrillin	antiplatelet drug

INDOLINE CONTAINING DRUG

NAME OF THE DRUG	STRUCTURE	COMPANY NAME	BRAND NAME	THERAPEUTIC APPLICATION
Sildenafil		Watson	Rapaflo	Treatment of benign prostatic hyperplasia

OXYINDOLE CONTAINING DRUG

NAME OF THE DRUG	STRUCTURE	COMPANY NAME	BRAND NAME	THERAPEUTIC APPLICATION
a) Ziprasidone		Pfizer	Geodon	Antipsychotic

b) <u>Ropinirole</u>		<u>Glaxosmithkline</u>	<u>Requip</u>	Treatment of Parkinson's disease
c) <u>Sunitinib</u>		<u>Pfizer</u>	<u>Sutent</u>	Treatment of renal cell carcinoma

CONCLUSION:

The present review summarizes all pharmacological aspects of the indole based molecules. A large number of drug molecules possessing indole nucleus, whether from natural origin or synthesized in laboratory, have been reported for the treatment of various disease conditions. Many of these molecules have been approved by FDA and are being currently utilized in drug therapies. We hope that in this review provides information regarding how the indole nucleus can be utilized by a medicinal chemist for the design and development of clinically viable molecules.

REFERENCES:

1. www.unb.br/iq/labpseq/qo/olv/olv/about. htm-23k
2. Srivastava A, Pandeya SN. Indole a versatile nucleus in pharmaceutical field, International Journal of current pharmaceutical review and research, 2011; 1[3]:1-17.
3. Lee JH, Lee J. Indole as an intercellular signal in microbial communities, FEMS Microbiology Reviews, 2009; 34[4]:426-44.
4. Cigdem K, Sibel S. Electrochemical Behavior of Biologically Important Indole Derivatives, International Journal of Electrochemistry, 2011; 110.
5. Bayer A. Concerning the reduction of aromatic compounds with zinc dust. European Journal of Organic Chemistry, 1866, 140[3]:295-96.
6. Bayer A., Emmerling A. Syntheses of indols, European Journal of Organic Chemistry, 1869; 2[1]:679-82.
7. Kurz WG, Chatson KB, Constabel F, Kutney JP, Choi LS, Kolodziejczyk P, Sleigh SK, Stuart KL, Worth BR. Alkaloid Production in Catharanthus roseus cell cultures VIII, Planta Medica, 1981; 42:22-31.
8. Leon F, Habib E, Adkins JE, Furr EB, McCurdy CR, Cutler SJ. Phytochemical characterization of the leaves of *Mitragyna speciosa* grown in U.S.A., Natural Product Communications, 2009; 4:907-10.
9. Ishikawa H, Colby DA, Boger DL. Direct coupling of catharanthine and vindoline to provide vinblastine: total synthesis of [b]- and ent- [-]-vinblastine, Journal of American Chemical Society, 2008; 130:420-21.
10. Freidonk ME, Fox A. Resolution of concentration response differences in onset of effect between subcutaneous and oral Sumatriptan, Headche, 2005; 45:632-37.
11. Generali JA, Cada. Off-lable drug uses- Indanetron: Postanesthetic shivering, Hospital Pharmacy, 2009; 44: 670-71.
12. Ferreira S, Moncada S, Vane J. Indomethacin and aspirin abolish prostaglandin release from the spleen, Nature: New Biology, 1971; 231:237-39.
13. Heba m. abo-salem*. Synthesis, antimicrobial activity and molecular docking study of some new *n*-benzyl and *n*-benzoyl-3-indolyl heterocycles international journal of pharmacy and pharmaceutical sciences ISSN- 2016;0975-1491 vol 8, issue 9
14. Adel hamed mandour et.al Synthesis and potential biological activity of some novel 3-[[*N*-substituted indol-3-yl]methyleneamino]-6-amino-4-aryl-pyrano[2,3-*c*]pyrazole-5-carbonitriles and 3,6-diamino-4-[[*N*-substituted indol-3-yl]pyrano[2,3-*c*]pyrazole-5-carbonitriles, *Acta Pharm.* 62 2012; 15-30 Original research paper DOI: 10.2478/v10007-012-0007.
15. Mari'a C. Copper complexes of imidazole-2-, pyrrole-2- and indol-3-carbaldehyde thiosemicarbazones: Inhibitory activity against fungi and bacteria Journal of Inorganic Biochemistry 99 2005; 2231-2239
16. Faritha a, Synthesis of certain thiazolyl-pyrazoline derivatives and evaluation of their antimicrobial activity unique research journal of chemistry 2014; 02 [03]: page 18-23
17. Jaiprakash S. Biradar, 2,5-Disubstituted novel indolyl pyrimidine analogues as potent antimicrobial agents, Der Pharmacia Lettre, 2012; 4 [1]:344-348
18. Saundane. reported the synthesis of 2- [2'5'-substituted indolide amino-3-yl] 4,b-diaryl pyrimidine possessing antibacterial activity. Journal of Chinese Chemical Society 2004; 51.147-156.
19. Asmaa S. Salman Synthesis, Reactions and Antimicrobial Activity of Some New 3-Substituted

Indole Derivatives, International Journal of Organic Chemistry

2015; Vol.05 No.02

20.S. N. Pandeya, P. Yogeeswari, D. Sriram and G. Nath, —Synthesis and antimicrobial activity of N-Mannich bases of 3-*N'*- sulphadoximino_ isatin and its methyl derivativel, *Boll. Chim. Farm.*137 1998; 321–324.

21.SüreyyaÖlgen,Nurten Altanlarb et. al.Synthesis and evaluation of novel N-H and N-substituted indole-2-and 3-carboxamide derivatives as antioxidants agents, *Sep* 2007; *Journal of Enzyme Inhibition and Medicinal Chemistry*

22.Dharmendra Kumar, Narendra Kumar, SandeepKumar, Tarun Singh, C. P. Singh, “Synthesis of pharmacologically active 2-phenyl sulphha/substituted Indolesl, *Int. J. Eng. Sci. and Tech.*, Vol. 2[7], 2010, 2553-2557.

23.Reddy A series of 1-[sulfanylphenyl]-3-trifluoromethyl-5-indolyipyrazolines were synthesized and evaluated as inhibitors of cyclooxygenase-II *Journal of Enzyme Inhibition and Medicinal Chemistry* 2008;

24.Rani P, Srivastava VK, Kumar A. Synthesis and anti-inflammatoryactivity of heterocyclic indole derivatives. *Eur J Med Chem.* 2004; 39:449-452.

25.Minakshi Shroff*1Newer Substituted Indolyl-Pyrazoline Derivatives as Anti-Inflammatory Agents *British medical bulletin*, 2017; Vol.5 No.1:298

26.S Muralikrishna Synthesis characterization and anti-inflammatory activity of indolederivatives bearing-4-oxazetidione, *Journal of Chemical and Pharmaceutical Research*, 2013; 5[10]:280-288

27.El-Sayed, Magda AA, Abdel-Aziz NI, Alaa AM, El-Azab AS, ElTahir KEH.Synthesis, biological evaluation and molecular modelling studyof pyrazole and pyrazoline derivatives as selective COX-2inhibitors and anti-inflammatory agents. *Bioorg Med Chem*,2012;20:3306–

28.Mohammad mumtaz alam1,Mmyoona akhter.,Anti-inflammatory and antimicrobial activity of 4,5-dihydropyrimidine-5-carbonitrile derivatives: their synthesis and spectral elucidation, *ActaPoloniaePharmaceutica ñ Drug Research*, 2012.; Vol. 69 No. 6 pp. 1077ñ1085,

29.Sally Synthesis, Antitumor and Anti-inflammatory Activities of 2-thienyl-3-substitued Indole Derivatives. *Mini Reviews in Medicinal Chemistry*, 2009; 782-793.

30.Mohammad Amir, SadiqueAkhtarJaved, Harish Kumar, —Synthesis and biological evaluation of some 4-[1H-indol-3-yl]-6phenyl-1, 2, 3, 4-tetrahydropyrimidin-2ones/thiones as potent antiinflammatory agentsl, *acta pharm*, 58 2008; 467–477.

31.Radwan, M.A. A.; Ragab, E.A.; Sabry, N. M.; Shenawy, S.M.E. *Bioorg Med Chem*, 1997; 15, 3832.

32.Ashok Kumar, —Thiazolyl/oxazolylformazanylindoles as potent anti-inflammatory agentsl *Eur. J. Med. Chem*, 43 2008; 2323-2330

33.Supriyamana, nilanjanpahari, neeraj k. sharma, priyanka, —synthesis and characterization of novel thiazoloisoxazole fused isatin as analgesic and anti-inflammatory agentl, *the pharma research [t. ph. res.]*,2010; 3; 51-59

34.Mohamed Jawed Ahsan, Synthesis and anticonvulsant activity of 3a,4-dihydro-3H-indeno[1,2-c]pyrazole-2-carboxamide/carbothioamide analogues, *Journal of Enzyme Inhibition and Medicinal Chemistry*, Volume 28, 2013; - Issue 3

35.Pravin ShahidShaikha, Naziabegum P.synthesis and antimicrobial activity of new 3, 4-dihydropyrimidinones via novel chalcone series, *Heterocyclic Letters*, May-July| 2015; Vol. 5 3

36.Slassi -Substitued indole of structure is an antagonist for receptor 5HT6 for the treatment of CNS disease, *J. Med. Chem.* 1965; 8: 397-398.]

37.Nadeem Siddiqui M. ShamsherAlam ,WaquarAhsa, — Synthesis, anticonvulsant and toxicity evaluation of 2-[1H-indol-3-yl]acetyl-N-[substitued phenyl]hydrazine carbothioamides and their related heterocyclic derivativesl *Acta Pharm*, 58 2008; 445–454

38.Abele, E.; Abele, R.; Dzenitis, O.; Lukevics, E. *Chem Heterocycl Compd*, 2003; 39, 3.

39.Abdou O Synthesis of New 3-Heteroarylindoles as Potential Anticancer Agents, *molecules*, July 2016.; 16

40.*Alshaimaa A. Bakr, et al.* synthesis and biological activity of certain new indole derivatives via the utility of2-acetylindole. *Bull. Pharmaceutical science Assiut University*, Dec -2006 ;vol-29: 348-370

41.Jing-Ping L, Kuo-Shun H, Ching-Chuan K, Chi-Yen C, Jang-Yang C. A novel oral indoline-sulfonamide agent, J30, exhibits potent activity against human cancer cells in vitro and in vivo through the disruption of microtubule. *JPET*2007; 323: 398-405.

42.Matthew SS, Tejas PP, Keith MG, Bryan EW. Synthesis and preliminary biological studies of 3-substitued indoles accessed by a palladium-catalyzedenantioselective alkene difunctionalization reaction. *J Am Chem Soc* 2010;132 [23]: 7870-7871.

43.Popp FD, Pajouhesh H. Potential anticonvulsants VI: Condensation of isatins withcyclohexanone and other cyclic ketones. *J Pharm Sci* 1983; 72: 318-321.

44.Doris K, Michaela P, Susanne V, Renate L, Robert G, Dietmar G, Tsuyuki N, Tobias P, Erwin VA. Antimitotic activities of 2-phenyl indole-3-

- carbaldehyde in human breast cancer cell. *Bioorg Med Chem* 2007; 15: 5122-5136.
45. Fan Z, Yanfang Z, Li S, Lu D, Yucheng G, Ping G. Synthesized in vitro antitumor activity of 2-amino-3-cyano-6-[1H-indol-3-yl]-4-phenylpyridine derivatives. *Eur J Med Chem* 2011; 46: 3149-3157.
46. Ulrich J, Nathalie D, Amelie L, Christian B, Cedric L, Jean-Michel R, Olivier Lh, Laurent M, Jean-Yves M, Sylvain R. Synthesized 3,5-bis[2-indolyl]pyridine and 3-[[2-indolyl]-5-phenyl]-pyridine derivatives as CDK inhibitors and cytotoxic agents. *Bioorg Med Chem* 2008; 16: 4932-4953.
47. Ekhlass N. Synthesis [in vitro] antitumor and antimicrobial activity of some pyrazoline, pyridine, and pyrimidine derivatives linked to indole moiety. *J Am Sci* 2010; 6[8]: 463-471.
48. Huasheng D, Chao Z, Xihan W, Chunhao Y, Xiongwen Z, Jian D, Yuyuan X. Novel indole α -methylene- γ -lactones as potent inhibitors for AKT-mTOR signaling pathway kinase. *Bioorg Med Chem Lett* 2009; 15: 4799-4802.
49. Magdy AHZ, Hanan FS, Yasmin GA, Amira MGE. Efficient microwave irradiation enhanced stereoselective synthesis and antitumor activity of indolylchalcones and their pyrazolineanalogs. *J Chem Sci* 2010; 122: 587-
50. Abdel-Rahman F. Synthesis of some new indole derivatives containing pyrazoles with potential antitumor activity. *Arkivoc* 2010; 11: 177-187.
51. Ahmed K, Srikanth YVV, Khan MNA, Shaik TB, Ashraf MD. Synthesis of 3,3-diindolyl oxyindoles efficiently catalysed by FeCl₃ and their in vitro evaluation for anticancer activity. *Bioorg Med Chem Lett* 2010; 20: 5229-5231.
52. Yu-Shan W, Mohane SC, Jang-Yang C, Hsu-Yi S, Fu-Ming K, Ching-Chuan K, Ying-Jun C, Chi-Yen C, Chia-Ling H, Jing-Ping L, Ching-Ping C, Hsien-Tsung Y, Yi-Kun C, Uan-Kang T, Chiung-Tong C, Chang-Ying C, Su-Ying W, Teng-Kuang Y, Chin-Yu L, Hsing-Pang H. Synthesis and evaluation of 3-aryloxyindoles as anticancer agents. *J Med Chem* 2009; 52: 4941-4945.
53. Palwinder S, Matinder K, Pooja V. Design, synthesis and anticancer activities of hybrids of indole and barbituric acids. *Bioorg Med Chem Lett* 2009; 19: 3054-3058.
54. Radulovic N. S.; Zlatkovic D. B.; Mitic K. V.; Randjelovic P. J.; Stojanovic N. M[2014]. Synthesis, spectral characterization, cytotoxicity and enzyme-inhibiting activity of new ferrocene-indole hybrid. *Polyhedron*; 2014; 80; 134-141.
55. Shchekotikhin A. E.; Glazunova V. A.; Dezhenkova L. G.; Luzikov Y. N.; Buyanov V. N.; Treshalina H. M.; Lesnaya N. A.; Romanenko V. I.; Kaluzhny D. N.; Balzarini J.; Agama K.; Pommier Y.; Shtil A. A.; Preobrazhenskaya M. N[2014]. Synthesis and evaluation of new antitumor 3-aminomethyl-4,11-dihydroxy-naphtho[2,3-f]indole-5,10-diones. *Eur. J. Med. Chem.*; 2014; 86; 797-805.
56. Guan Q.; Han C.; Zuo D.; Zhai M.; Li Z.; Zhang Q.; Zhai Y.; Jiang X.; Bao K.; Wu Y.; Zhang W[2014]. Synthesis and evaluation of benzimidazole carbamates bearing indole moieties for anti-proliferative and anti-tubulin activities. *Eur. J. Med. Chem.*; 2014; 87; 306-315.
57. Jun-Rong Jiang, Feng Xu, and Han-Gui Wu; Synthesis and Anticancer Activity of 1-[1H-Indol-3-yl]-2-[4-diarylmethylpiperazine-1-yl]ethane-1,2-dione Derivatives, *Journal of Chemistry*, Volume 2016 2016; Article ID 4617454, 5 pages
58. Wen-Tai, Li. Der-Ren Hwang, Ching-Ping Chen, Chien-Wei Shen, Chen-Long Huang, Tung-Wei Chen, Chi-Hung Lin, Yee-Ling Chang, Ying-Ying Chang, Yue-Kan Lo, Huan-Yi Tseng, Chu-Chung Lin, Jeng-Shin Song, Hua-Chien Chen, Shu-Jen Chen, Se-Hui Wu, Chiung-Tong **Chem. J. Med. Chem., 2003;46[9], pp 1706-1751.**
59. Roy S, Eastman A, Gribble GW. Synthesis of bisindolylmaleimides related to GF109203x and their efficient conversion to the bioactive indolocarbazoles. *Org Biomol Chem* 2006; 4: 3228-3234.
60. Enien, H.Y.A; Kruk, I.; Lichtszeld, K.; Olgen, S., *Luminescence*, 2004;19,1.
61. Talaz, O.; Gulcin, I.; Goksu, S.; Saracoglu, N. *Bioorg Med. Chem.* 2009;17,6583
62. Periyasamy Selvam, Narayanan Murugesu, Markandavel Chandramohan, Robert W Sidwell, Miles K Wandersee and Donald F Smees, —Antiviral Chemistry & Chemotherapy, Anti-influenza activities of isatid derivatives, *Int. Medical Press*, 2006;
63. Ping GONG, Dun WANG, De Sheng YU, Fang QIN, Lin FANG, —Synthesis and *In Vitro* Antiviral Activities of Some New 2-Arylthiomethyl-4-tertiaryaminomethylsubstituted Derivatives of 6-Bromo-3-ethoxycarbonyl-5-hydroxyindoles, *Chinese Chemical Letters*, 2004; Vol. 15, No. 1, pp 19 – 22
64. Abele, E.; Abele, R.; Dzenitis, O.; Lukevics, E. *Chem Heterocycl Compd*, 2003;39, 3.
65. *Heterocyclic Scaffolds II: 2010 Reactions and Applications of Indoles* Editors: Gribble, Gordon W. [Ed.].