

INDOLE: THE MOLECULE OF DIVERSE PHARMACOLOGICAL ACTIVITIES

Jonnakuti Poojitha*, Kanneti Naga Mounika, Gollapalli Naga Raju, Rama Rao
Nadendla

Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences,
Guntur, Andhra Pradesh, India.

Article Received on
02 Oct 2015,

Revised on 23 Oct 2015,
Accepted on 12 Nov 2015

***Correspondence for
Author**

Jonnakuti Poojitha
Department of
Pharmaceutical Analysis,
Chalapathi Institute of
Pharmaceutical Sciences,
Guntur, Andhra Pradesh,
India.

ABSTRACT

Indole, the bicyclic ring system consists of pyrrole ring fused with benzene ring. 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. A large number of efforts were made to synthesize different indole compounds and their derivatives in the past decade and were found to numerous pharmacological activities like antitumor, anticonvulsant, antimicrobial, anthelmintic, antileishmanial, anti-tubercular, schistosomicidal, antifungal, anti-inflammatory antipsychotic and anti diabetic activities. Due to its wider applications in pharmaceutical industries, they will replace many existing heterocyclic based pharmaceuticals. Now days, many drugs are in the world market, while several hundred are in clinical trials. The present review focuses on the indole with potential activities that are now in development.

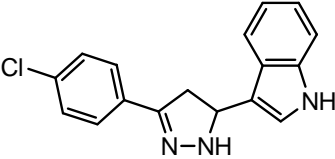
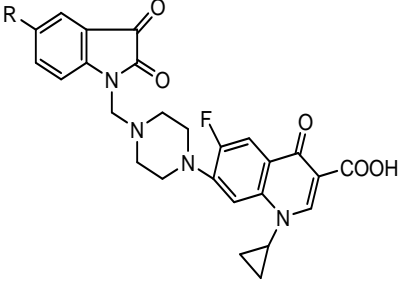
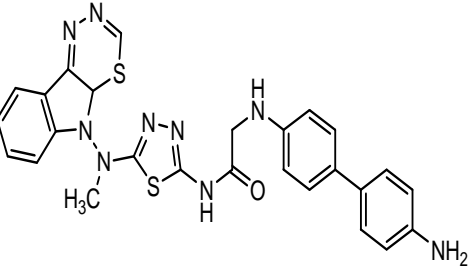
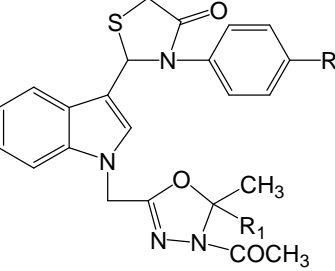
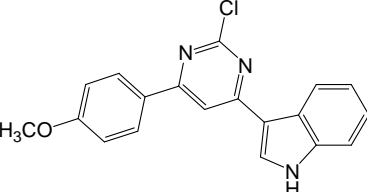
KEYWORDS: Indole, Analgesic, Anticancer, Antimicrobial, Anticonvulsant.

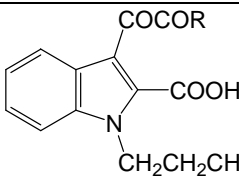
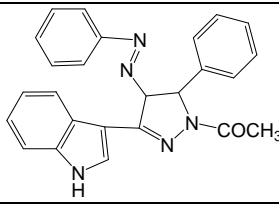
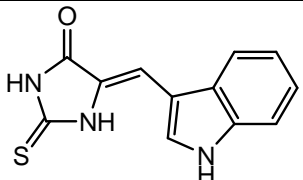
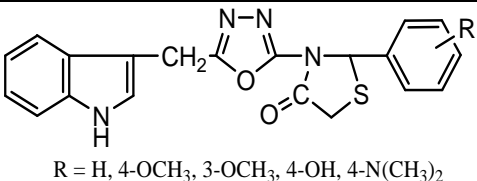
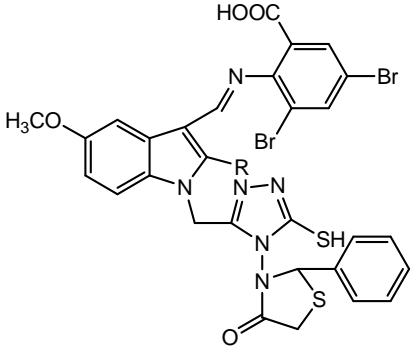
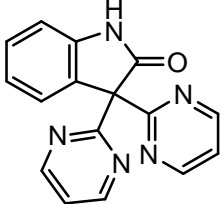
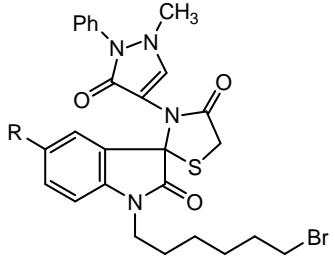
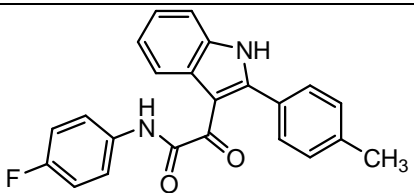
INTRODUCTION

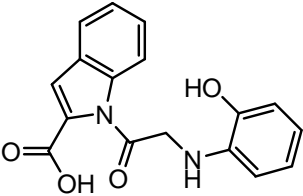
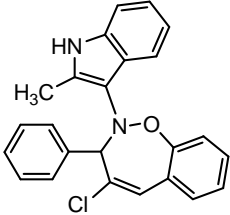
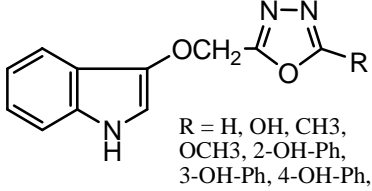
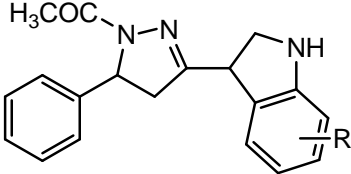
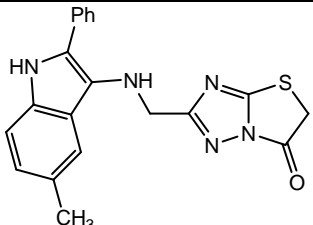
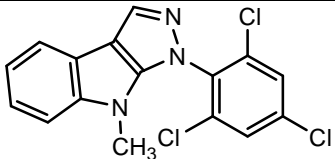
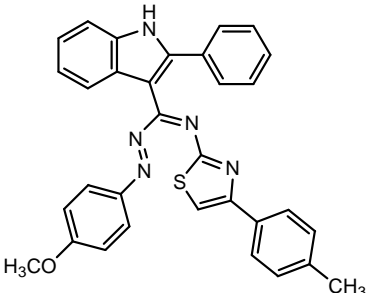
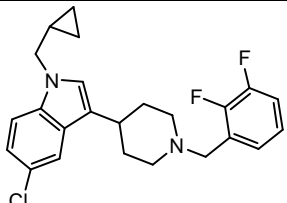
Heterocyclic compound is one which possesses a cyclic structure with at least one hetero atom in the ring. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. The chemistry and biological study of heterocyclic compounds has been an interesting field for a long time in medicinal chemistry. A number of heterocyclic derivatives containing nitrogen atom serve as a unique and versatile scaffolds for experimental drug design. Indole is a heterocyclic compound, is made from pyrrole ring

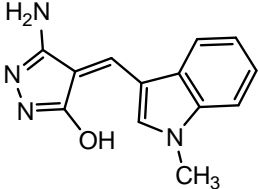
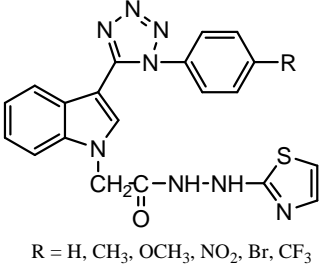
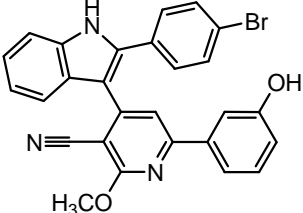
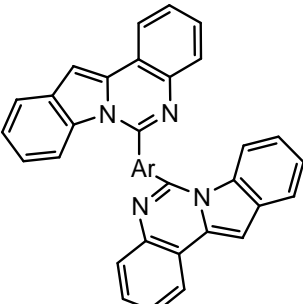
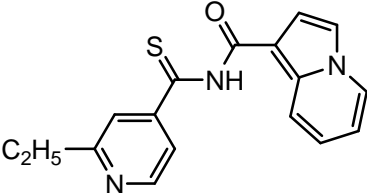
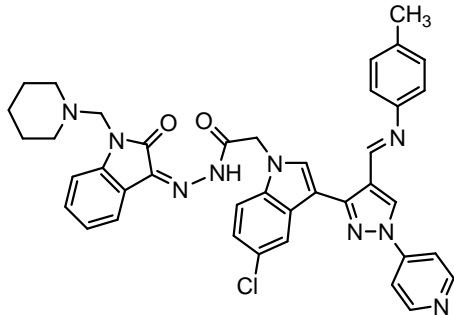
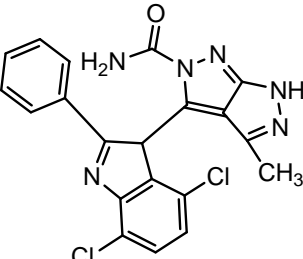
fused with benzene ring, having various biological activities and still of great scientific interest now a days.

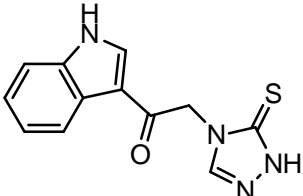
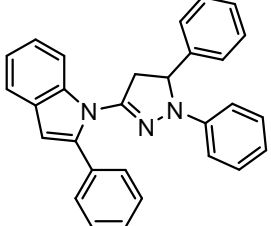
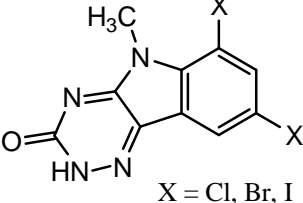
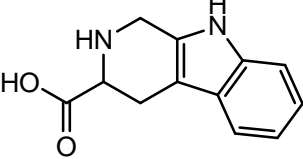
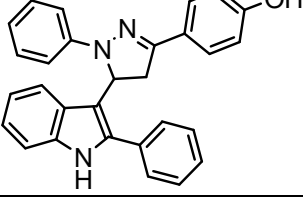
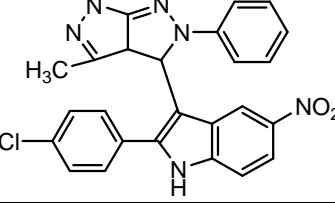
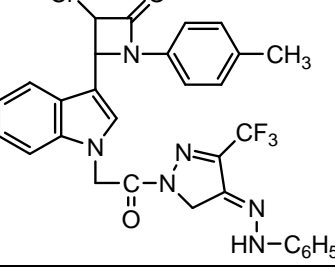
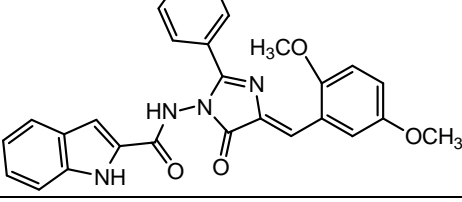
Indole compounds and their derivatives were found to numerous pharmacological activities like antitumor^[1], anticonvulsant^[2], antimicrobial^[3], anthelmintic^[4], antileishmanial^[5], anti-tubercular^[6], antioxidant^[7], antifungal^[8], anti-inflammatory^[9] and antipsychotic^[10] activities. The present review focuses on the Indole moiety with potential activities that are now in development.

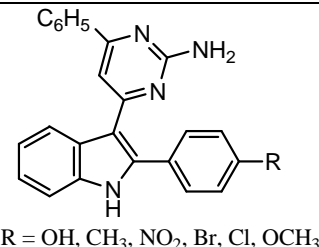
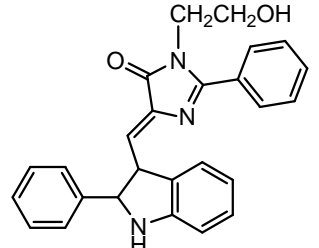
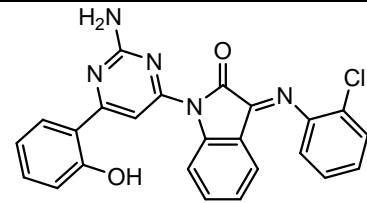
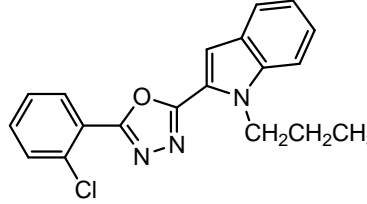
S.No	Author	Derivatives	Activity	Ref. No
1	Pravin O. Patil and Sanjay B. Bari		Antidepressant and Anticonvulsant activity	[11]
2	Avinash Rangaraju et al		Antimycobacterial	[12]
3	Hemant Panwar et.al		Antifungal and Antibacterial	[13]
4	S. Muralikrishna et al.		Anti-inflammatory	[14]
5	Ekhlass Nassar		Antitumor	[15]

6	Gollapalli Naga Raju et al		Antibacterial and Antifungal	[16]
7	Ashok S. Narute et al		Anti-inflammatory	[17]
8	A.S.H. da Silva Guerra et al		Anti-inflammatory and antinociceptive	[18]
9	Singh <i>et al.</i>	 R = H, 4-OCH ₃ , 3-OCH ₃ , 4-OH, 4-N(CH ₃) ₂	Cardiovascular Activity	[19]
10	Ashok Kumar et al		Anti-inflammatory	[20]
11	Parvaneh Pakravan et al.		Anticancer activity	[21]
12	R. Sakhuja et al.		Antimicrobial activity	[22]
13	Cinchana NV, Sujan Ganapathy PS and Shruthi SD		Antioxidant and antibacterial activities	[23]

14	Nagaraja naik, V. et al		Antioxidant	[24]
15	Anil Kumar <i>et al</i>		Anticonvulsant	[25]
16	Harish Rajak <i>et al</i>	 R = H, OH, CH ₃ , OCH ₃ , 2-OH-Ph, 3-OH-Ph, 4-OH-Ph,	Anticonvulsant	[26]
17	Ashok S. Narute et al	 R = H, NO ₂ , OH, OCH ₃ , CH ₃ , Cl, Br	Anti-inflammatory activity	[27]
18	Saundane <i>et al.</i>		Antioxidant and antibacterial activities	[28]
19	A. H. Mandour <i>et al</i>		Anti-inflammatory, Analgesic and Anticonvulsant activities	[29]
20	Saundane anand et al		Antioxidant, Antimicrobial, Antimycobacterial and Cytotoxic agents	[30]
21	Mahadevan et al		Anti-histaminic activity	[31]

22	S. Jain., B. N. Reddy and K. S. Rao		Antibacterial Activity	[32]
23	S. Muralikrishna et.al,	 R = H, CH ₃ , OCH ₃ , NO ₂ , Br, CF ₃	Antimicrobial activity	[33]
24	Hardik M. Patel, Nilesh Darji, Jagath Pillai		Anticancer activity	[34]
25	Rondla Rohini P. Muralidhar Reddy, Kanne Shanker, Anren Hu and Vadde Ravinder		Antimicrobial activity	[35]
26	Srikanth Lingala, Raghunandan Nerella, Ratnakar Cherukupally, Amit k. Das		Anti tubercular activity	[36]
27	J. Sreeramulu et al		Antimicrobial activity	[37]
28	J. Sreeramulu et al		Antimicrobial activity	[38]

29	Rohini R M et al		anti-convulsant activity	[39]
30	Chavan Rajashree et al		Analgesic & anti-inflammatory activities	[40]
31	Rajeev Kumar et al	 X = Cl, Br, I	Anticonvulsant Activity	[41]
32	Ramninder Kaur, Mandeep Kaur, Komalpreet Kaur		Antimicrobial activity	[42]
33	R.S. Chavan et al		Anti-inflammatory	[43]
34	P. Ashok Gajapathi Raju <i>et al</i>		Antimicrobial activity	[44]
35	S. Muralikrishna <i>et al</i>		Anti-inflammatory	[45]
35	Gollapalli Naga Raju <i>et al</i>		Antimicrobial activity	[46]

36	Rajashree S Chavan et al	 <p>R = OH, CH₃, NO₂, Br, Cl, OCH₃</p>	Analgesic and Anti-inflammatory	[47]
37	Asif Husain et al		Anticonvulsant Activity	[48]
38	Prasenjit Mondal et al		Antioxidant & Antibacterial	[49]
39	Gollapalli Naga Raju et al		Antimicrobial activity	[50]

CONCLUSION

The different type of Indole derivatives is shown a wide spectrum of biological activities. The plethora of research described in this review indicates the wide spectrum of biological activities exhibited by Indole derivatives. The biological profiles of these new generations of indoles would represent a fruitful matrix for further development of indole nucleus, which can be a lead nucleus for future developments to get safer and effective therapeutic agents.

ACKNOWLEDGEMENT

The authors are grateful to Department of Pharmaceutical Analysis, Chalapathi Institute of Pharmaceutical Sciences, Guntur for providing facilities to perform the review work.

REFERENCES

1. S. Muralikrishna et al, Synthesis Characterization and antitumor activity of thiazole derivatives containing indole moiety bearing-tetrazole; Der Pharma Chemica, 2013; 5(6): 87-93.
2. Rohini R M et al, Synthesis and anti-convulsant activity of triazothiole/thiazolyl thiazolidinone derivatives of indole; Der Pharma Chemica, 2012; 4(6): 2438-2441.

3. Gollapalli Naga Raju et al, Synthesis, characterization and biological activity of some 1,3,4-oxadiazole derivatives with indole moiety; *Der Pharmacia Lettre*, 2015; 7(5): 153-159.
4. Mondal P, Jana S, Balaji A, Ramakrishna R, Kanthal LK. Synthesis of some new isoxazoline derivatives of chalconised indoline 2-one as a potential analgesic, antibacterial and anthelmimtic agents; *J Young Pharmacists*, 2012; 4: 38-41.
5. Delorenzi et al, Antileishmanial Activity of an Indole Alkaloid from *Peschiera australis*; *Antimicrobial Agents And Chemotherapy*, May 2001; 45(5): 1349–1354.
6. Prabhaker Walmik and Saundane A. R, Synthesis of novel indolyl-azetidinone and thiazolidinone derivatives as a potent antioxidant, antimicrobial and antitubercular agents; *Der Pharma Chemica*, 2014; 6(4): 70-79.
7. Monica S. Estevao et al, Antioxidant activity of unexplored indole derivatives: Synthesis and screening; *European Journal of Medicinal Chemistry*, November 2010; 45(11): 4869–4878.
8. P. Ashok Gajapathi Raju et al, Synthesis and biological activity of some new indole derivatives containing pyrazole moiety; *J. Chem. Pharm. Res.*, 2013; 5(10): 21-27.
9. A.S.H. da Silva Guerra et al, Anti-inflammatory and antinociceptive activities of indole – imidazolidine derivatives; *International Immunopharmacology*, 2011; 11: 1816–1822.
10. Mahadevan et al, Synthesis and Docking Study of 3-(N-Alkyl/Aryl Piperidyl) Indoles with Serotonin-5HT₁, H₁ and CCR2 Antagonist Receptors; *Int J Pharm Pharm Sci*, 6(4): 475-482.
11. Patil, P.O., Bari, S.B. Synthesis, characterization and screening for antidepressant and anticonvulsant activity of 4,5-dihydropyrazole bearing indole derivatives; *Arabian Journal of Chemistry*, 2013; 1-8.
12. Avinash Rangaraju et al, Synthesis of Novel 1H- Indole-2, 3-Dione Derivatives as potent Antimycobacterial Agents; *IJAPBC – Oct-Dec*, 2013; 2(4).
13. Hemant Panwar et.al, Synthesis, characterization and biological activity of some substituted pyrazolyl and pyrazolinyl-1, 3, 4-thiadiazino (6,5-b) indoles; *Rasayan. J. chem.*, 2011; 4(2): 371-380.
14. S. Muralikrishna et al., Synthesis of 1,3,4 Oxadiazole derivatives containing Indole moiety bearing-Thiazolidinone and Anti-inflammatory activity of Thiazolidinone; *Int. J. Chem Tech Res.*, 2014; 6(1): 183-194.

15. Ekhllass Nassar, Synthesis, (in vitro) Antitumor and Antimicrobial Activity of some Pyrazoline, Pyridine, and Pyrimidine Derivatives Linked to Indole Moiety; *Journal of American Science*, 2010; 6(8): 338-347.
16. Gollapalli Naga Raju et al, Synthesis, Characterization and biological activity of indole-2-carboxylic acid derivatives; *IJPC*, 2015; 05(06): 201-206.
17. Ashok S. Narute et al, QSAR Study on 3-Substituted Indole Derivatives as Anti-Inflammatory Agents; *Int J Pharm Bio Sci*, 2013 July; 4(3): 482 – 492.
18. A.S.H. da Silva Guerra et al, Anti-inflammatory and antinociceptive activities of indole–imidazolidine derivatives; *International Immunopharmacology*, 2011; 11: 1816–1822.
19. Singh et al, Synthesis and Evaluation of Some Substituted Indole Derivatives for Cardiovascular Activity; *International Journal of Pharmaceutical Sciences and Drug Research*, 2013; 5(1): 14-17.
20. Ashok Kumar et al, Synthesis and Anti-inflammatory Activity of Indole Derivatives; *Int.J. Chem Tech Res.*, April-June 2010; 2(2): 762-773.
21. Parvaneh Pakravan et al, Biochemical and pharmacological characterization of isatin and its derivatives: from structure to activity; *Pharmacological Reports*, 2013; 65: 313-335.
22. R. Sakhuja et al, Design and synthesis of spiro[indole-thiazolidine]spiro[indole-pyrans] as antimicrobial agents; *Bioorganic & Medicinal Chemistry Letters*, 2011; 21: 5465–5469.
23. Cinchana NV, Sujana Ganapathy PS and Shruthi SD, In- vitro antioxidant and antibacterial activities of the four synthesized indole derivatives; *RJPBCS*, April – June 2011; 2(2): 353-362.
24. Nagaraja naik, V. Sharath, H. Vijay kumar and H. Swetha, Synthesis and In Vitro Antioxidant Evaluation of Some Indole-2-carboxylic Acid-Aryl Amine Conjugates; *Chem Sci Trans.*, 2013; 2(1): 113-122.
25. Anil Kumar et al, Synthesis and Evaluation of Some Newer Indole Derivatives As Anticonvulsant Agents; *International Journal of Pharmaceutical & Biological Archives*, 2011; 2(2): 744-750.
26. Harish Rajak et al, Synthesis and Pharmacological evolution of new indolyl –oxadiazole as Anticonvulsant agents; *Int J Pharm Bio Sci.*, 2009; 2(3): 661-667.
27. Ashok S. Narute et al, QSAR Study on 3-Substituted Indole Derivatives as Anti-Inflammatory Agents; *Int J Pharm Bio Sci.*, 2013 July; 4(3): 482 – 492.
28. Saundane et al, Synthesis and Biological Activities of Some Indole Analogues Containing Triazole-5-Thiol and Thiazolotriazole Systems; *Int J Pharm Pharm Sci*, 6(10): 534-539.

29. H. Mandour et al.: Synthesis, anti-inflammatory, analgesic and anticonvulsant activities of 1,8-dihydro-1-aryl-8-alkyl pyrazolo-(3,4-b)indoles; *Acta Pharm.*, 2010; 60: 73–88.
30. Saundane anand et al., Synthesis of Novel N-(Aryl) diazenyl thiazol-2-amines and Bezyliidenethiazolidin-4-ones linked to Indole Nucleus as Antioxidant, Antimicrobial, Antimycobacterial and cytotoxic agents; *Int J Pharm Pharm Sci*, 6(2): 141-147.
31. Mahadevan et al., Synthesis and Docking study of 3-(N-alkyl/aryl piperidyl) indoles with Serotonin-5HT, H1 and CCR2 antagonist receptors; *Int J Pharm Pharm Sci*, 6(4): 475-482.
32. S. Jain., B. N. Reddy, and K. S. Rao, Synthesis of Biheterocycles Containing Indole Nucleus and Their Antibacterial Activity; *J. Sci. Res.*, 2012; 4(1): 273-278.
33. S. Muralikrishna et.al, Synthesis Characterization and Biological Evaluation of Novel Thiazole Derivatives Containing Indole Moiety Bearing-Tetrazole; *International Journal of Pharma Research & Review*, Feb 2014; 3(2): 58-64.
34. Hardik M. Patel, Nilesh Darji, Jagath Pillai, Bhagirath Patel, Design, Synthesis and Anticancer Activity of 2-Phenyl-1H Indole Derivatives; *International Journal of Institutional Pharmacy and Life Sciences*, July-August 2012; 2(4).
35. Rondla Rohini P. Muralidhar Reddy, Kanne Shanker, Anren Hu and Vadde Ravinder, Synthesis of Some New Mono, Bis-Indolo[1, 2-c]quinazolines: Evaluation of their Antimicrobial Studies; *J. Braz. Chem. Soc.*, 2010; 21(5): 897-904.
36. Srikanth Lingala, Raghunandan Nerella, Ratnakar Cherukupally, Amit k. Das; Synthesis and Comparative Anti-Tubercular Activity of Indolizine Derivatives Of Isoniazid/Pyrazinamide/Ethionamide; *International Journal of Pharmaceutical Sciences Review and Research*, January – February 2011; 6(2): Article-023, 128-131.
37. J. Sreeramulu et al; Synthesis, characterization and antimicrobial activity of novel mannich bases of indol derivatives; *Der Chemica Sinica*, 2014; 5(2): 51-61.
38. J. Sreeramulu et al, Synthesis of some new pyrazolo-pyrazole derivatives containing indoles with antimicrobial activity; *Der Pharma Chemica*, 2011; 3(5): 301-309.
39. Rohini R M et al; Synthesis and anti-convulsant activity of triazothiole/thiazolyl thiazolidinone derivatives of indole; *Der Pharma Chemica*, 2012; 4(6): 2438-2441.
40. Chavan Rajashree et al; Synthesis and Biological Evaluation of Novel Series of 1-(4, 5-Dihydropyrazolyl) – Indoles; *Der Pharmacia Lettre*, 2012; 4(4): 1236-1245.
41. Rajeev Kumar et al, Design, Synthesis and Anticonvulsant Activity Of Some New 6,8-Halo-Substituted-2H-[1,2,4]triazino[5,6-B]indole-3(5H)-one/-thione and 6,8-halo-

- substituted 5-methyl-2H-[1,2,4]triazino[5,6-B]indol-3(5H)-one/-thione; EXCLI Journal, 2014; 13: 225-240.
42. Ramninder Kaur, Mandeep Kaur, Komalpreet Kaur; Synthesis and Biological Evaluation of 1, 2, 3, 4-Tetrahydro-9H-Pyrido [3, 4-B] Indole-3-Carboxylic Acid; International Journal of Drug Formulation and Research, Jan-Feb.2013; 4(1).
43. R.S. Chavan et al., Synthesis and evaluation of analgesic and anti-inflammatory activities of a novel series of 3-(4, 5-dihydropyrazolyl)-indoles; Int J Pharm Biomed Res., 2010; 1(4): 135-143.
44. P. Ashok Gajapathi Raju et al; Synthesis and biological activity of some new indole derivatives containing pyrazole moiety; J. Chem. Pharm. Res., 2013; 5(10): 21-27.
45. S. Muralikrishna et al; Synthesis characterization and anti-inflammatory activity of indole derivatives bearing-4-oxazetidinone; J. Chem. Pharm. Res., 2013; 5(10): 280-288.
46. Gollapalli Naga Raju et al; Synthesis, characterization and biological evaluation of indole-2-carboxamides fused with imidazolinone moiety; Der Pharmacia Lettre, 2015; 7(6): 31-36.
47. Rajashree S Chavan et al; Synthesis, Characterization and Evaluation of Analgesic and Anti-inflammatory Activities of Some Novel Indoles; Tropical Journal of Pharmaceutical Research, August 2011; 10(4): 463-473.
48. Asif Husain et al; Synthesis and Anticonvulsant Activity of Indolo-Imidazolone Hybrid Molecules; RRJOMC, March-April, 2015; 1(1): 23-28.
49. Prasenjit Mondal et al; Synthesis Of Novel Mercapto-Pyrimidine And Amino-Pyrimidine Derivatives Of Indoline-2-One As Potential Antioxidant & Antibacterial Agents; The Pharma Research (T. Ph. Res.), 2010; 3: 17-26.
50. Gollapalli Naga Raju et al; Synthesis, characterization and biological activity of some 1,3,4-oxadiazole derivatives with indole moiety; Der Pharmacia Lettre, 2015; 7(5): 153-159.