



AMERICAN JOURNAL OF PHARMTECH RESEARCH

Synthesis and Evaluation of 4-(2-Chloroquinolin-3-Yl)-6-(6-Methyl-1H-Benzimidazol-2-Yl)Pyrimidin-2-Amines as Potent Anthelmintic Agents

B. Shivakumar*, Indira. M. Madawali, Shivakumar Hugar and Navanath. V. Kalyane
*Department of Pharmaceutical Chemistry, B.L.D.E.A's SSM College of Pharmacy and
Research Centre, Vijayapur, Karnataka-586103, India.*

ABSTRACT

A new series of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl)pyrimidin-2-amine (Va-k) have been synthesized by the reaction of 3-(2-chloroquinolin-3-yl)-1-(6-methyl-1H-benzimidazol-2-yl)prop-2-en-1-one (IVa-k) with guanidine nitrate in ethanol and aqueous solution of sodium hydroxide. The synthesized compounds were characterized by their IR, ¹H NMR and Mass spectral studies. The synthesized compounds were evaluated for anthelmintic activity by in-vitro method, against south Indian adult earth worms *Pheretima posthuma* using Albendazole as a standard drug. Results of the activities reveal that, compounds exhibited moderate to good anthelmintic activity.

Keywords: 6-Methylbenzimidazoles, Chalcones, Pyrimidines, Albendazole, Anthelmintic activity.

*Corresponding Author Email drbsk_2007@yahoo.com

Received 01 October 2018, Accepted 23 October 2018

Please cite this article as: Sivakumar B *et al.*, Synthesis and Evaluation of 4-(2-Chloroquinolin-3-Yl)-6-(6-Methyl-1H-Benzimidazol-2-Yl)Pyrimidin-2-Amines as Potent Anthelmintic Agents. American Journal of PharmTech Research 2018.

INTRODUCTION

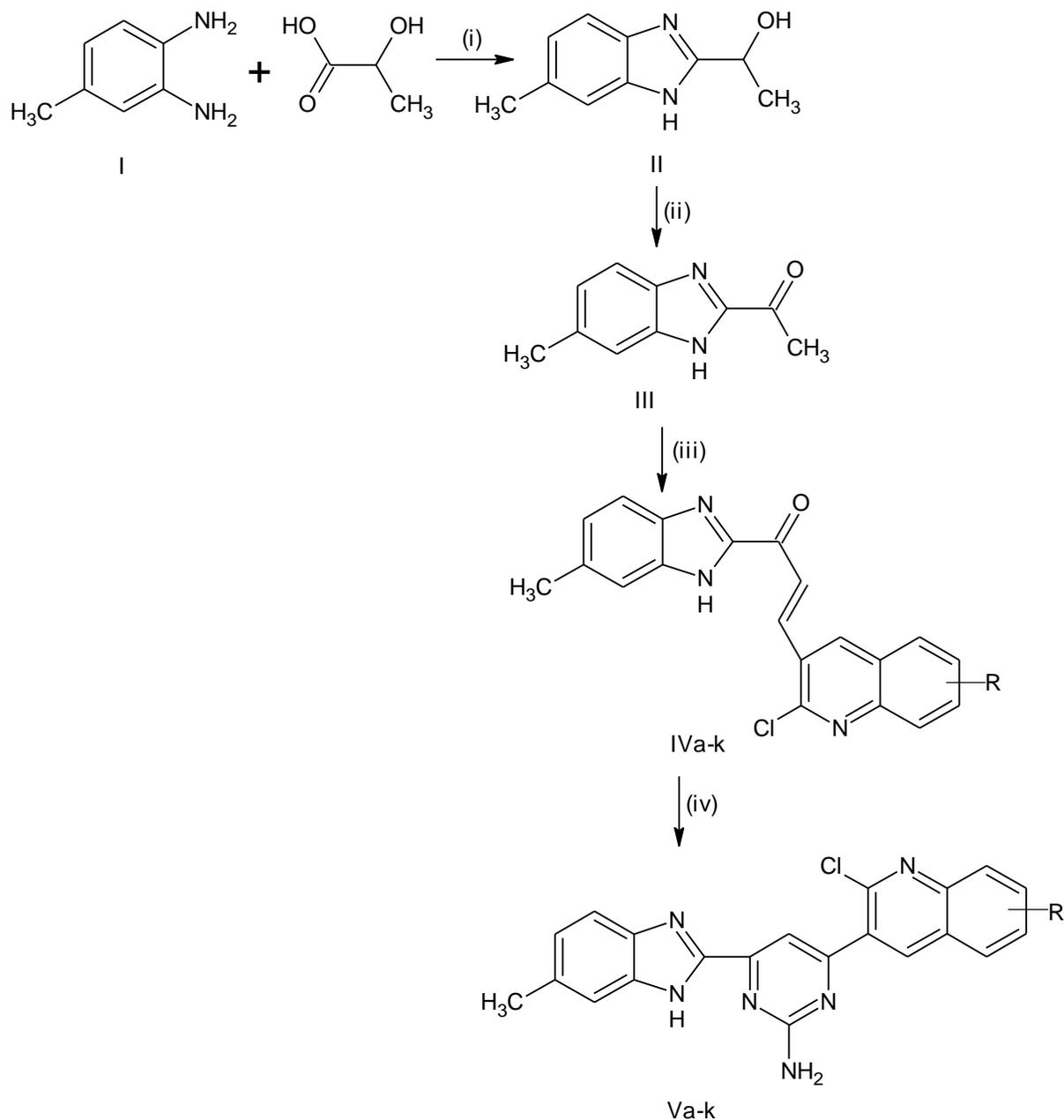
Benzimidazole derivatives are very useful intermediates/subunits for the development of molecules of pharmaceutical or biological interest [1]. Substituted benzimidazole derivatives have been found to be used in a variety of therapeutic areas including antimicrobial [2], antioxidant [3], antiviral [4], anti hypertensive [5], antiprotozoal [6], anti-inflammatory [7] and anti-filarial agents [8].

Nitrogen-containing heterocycles are a key class of compounds in medicinal chemistry and also contribute to the community from the biological and industrial point of view that helps in understanding life processes. The chemistry of the pyrimidines and their derivatives has been studied since the last century due to their various pharmacological properties and their close pharmacological associations. This is because the pyrimidine represents one of the most active classes of compounds with a broad spectrum of biological activity [9].

Pyrimidine ring complexes have been found to be an important part of Agrochemicals and veterinary medicinal products with various heterocyclic molecules and natural products. The fused pyrimidine derivatives have attracted the attention of many researchers for many years due to their important biological activities [10]. Preclinical data obtained from the literature research suggest that together with pyrimidine, heterocycles exhibit good antimicrobial, antioxidant, anti-inflammatory, analgesic and antipyretic, anti-tumor activities.

Anthelmintics or antihelminthics are drugs that expel helminth parasitic worms (helminths) from the body either by stunning or killing them. They may also be called verminfuges (stunning) or vermicides (killing). They have, however, demonstrated the development of resistance to some broad-spectrum anthelmintics (benzimidazoles, levamisol, avermectins) and some narrow-spectrum dewormers such as salicyllanilides (closantel). Some dangerous helminths infections, such as filariasis, currently have only a few treatment modalities. A continuous and long-term dependence on very few compounds has led to the development of drug resistance in many helminthic strains. In addition, several side effects have been reported in hosts such as gastrointestinal symptoms (epigastric pain, diarrhea, nausea, vomiting), nervous system symptoms (headache, dizziness) and allergic phenomena (edema, rashes, urticaria) after treatment with albendazole or mebendazole. Some anthelmintic drugs such as praziquantel and albendazole are contraindicated for some groups of patients, such as pregnant and lactating women. These drugs should also be used with caution in hepatitis patients and children under 2 years of age. In order to overcome the development of drug resistance, it is very important to synthesize a new class of compounds with different chemical properties than those commonly used [11].

Therefore, this study was designed to synthesize new sequences of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl)pyrimidin-2-amines as strong anthelmintic agents by adopting standard procedure.



Scheme

R= (a)-H; (b)-6-CH₃; (c)-7-CH₃; (d)-8-CH₃; (e)-6- OCH₃; (f)-7- OCH₃; (g)-8- OCH₃; (h)-6-Cl; (i)-7-Cl; (j)-6-Br; (k)-6-F.

Reagents and conditions:- (i) Lactic acid, 4N HCl, MW irradiation 320 minutes (ii) $K_2Cr_2O_7$, H_2SO_4 (25% v/v) 2 hrs, (iii) 10% NaOH, 2-chloroquinoline-3-carbaldehydes, Ethanol, 0.5 hrs, (iv) Guanidine nitrate, Ethanol, NaOH (40%), 10 hrs.

EXPERIMENTAL SECTION:

By open capillary tube method, melting points were checked and are uncorrected. By using TLC plates, TLC analysis was performed. By using KBr method, on a Shimadzu FTIR 8400S spectrometer IR spectra were recorded. On Bruker Avance II of 400 MHz NMR spectrometer, NMR spectra and Mass spectra on a Waters, Q-TOF Micro ma SS spectrometer were recorded.

Synthesis of 1-(6-methyl-1*H*-benzimidazol-2-yl) ethanol (II)

4-methyl-o-phenylenediamine (0.01,mole) (I) was mixed with Lactic acid (0.01 mole) and 4N hydrochloric acid under Phillips conditions and heated to reflux in a synthetic microwave system, at an intensity of 65% (450 W) for 320 minutes. TLC was monitored, after completion of reaction period; cooled mixture was neutralized by sodium bi carbonate. The solid was separated, filtered and recrystallization was carried out from absolute alcohol. m.p-186-88° [12, 13, 14].

Synthesis of 1-(6-methyl-1*H*-benzimidazol-2-yl) ethanone (III)

To a solution of 1-(6-methyl-1*H*-benzimidazol-2-yl)ethanol (II) (8.8g, 50 mmole) in dilute H_2SO_4 (5%, 40 ml) was added a solution of $K_2Cr_2O_7$ (44g, 150 mmole) in dilute H_2SO_4 (25%, 80 ml) with constant stirring, drop wise for 20 minutes at an ambient temperature. The stirring further continued for 2 hours. On completion of reaction period (TLC monitored), separated solid (a chromium complex) dispersed in water and adjusted a pH up to 6 to 6.5 with aqueous ammonia (1:1). Solid product then washed, dried and recrystallized by ethyl acetate to obtain a purified compound. m.p-195-97° [15, 16].

Synthesis of 3-(2-chloroquinolin-3-yl)-1-(6-methyl-1*H*-benzimidazol-2-yl) prop-2-en-1-one (IVa-k)

1-(6-methyl-1*H*-benzimidazol-2-yl) ethanone (III) (10 mmole, 1.74g) and substituted 2-chloroquinoline-3-carbaldehydes (10 mmole, 1.91g) were mixed in 30 ml of aqueous NaOH (10%). Continuing stirring up to 30 minutes, TLC was checked for completion of reaction. Solid filtered was dried. In addition, purified by recrystallization from a suitable solvent [17-23].

Similarly, 3-(2-chloroquinolin-3-yl)-1-(6-methyl-1*H*-benzimidazol-2-yl) prop-2-en-1-one (IVa-k) were synthesized.

IVb: yield 77%, m.p-250-52°; IR (KBr): 3275, 3064, 2918, 1658, 1579, 1427, 1217, 763 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz): δ 2.52 (s, 3H, CH_3), 2.79 (s, 3H, CH_3), 5.14 (s, 1H, NH-benzimidazole),

6.63 (d, 1H, 1-ethylene), 7.73 (d, 1H, 1-ethylene), 7.10-7.68 (m, 3H, Benzimidazole), 7.29-8.52 (m, 4H, Quinoline). MS: m/z 361.80 ($M^{+\bullet}$).

IVe: yield 86%, m.p-262-64 $^{\circ}$; IR (KBr): 3271, 3192, 2848, 1664, 1554, 1234, 804 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz): δ 2.49 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 5.14 (s, 1H, NH-benzimidazole), 6.63 (d, 1H, 1-ethylene), 7.73 (d, 1H, 1-ethylene), 7.07-7.37 (m, 3H, Benzimidazole), 7.52-8.53 (m, 4H, Quinoline). MS: m/z 377.80 ($M^{+\bullet}$).

IVh: yield 88%, m.p-278-80 $^{\circ}$; IR (KBr): 3282, 2850, 1660, 1566, 1413, 1334, 802, 719 cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz): δ 2.30 (s, 3H, CH_3), 5.21 (s, 1H, NH-benzimidazole), 6.58 (d, 1H, 1-ethylene), 7.18 (d, 1H, 1-ethylene), 7.04-7.49 (m, 3H, Benzimidazole), 7.67-8.23 (m, 4H, Quinoline). MS: m/z 382.20 ($M^+ + 1$).

Synthesis of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl) pyrimidin-2-amine (Va-k)

In ethanol (25 ml), add a chalcone derivative (4) (3.68g, 0.01 mole) and guanidine nitrate (1.80g, 0.01 mole). An aqueous solution of sodium hydroxide (40%, 5ml) was added portion wise during a period of 3 hours. Refluxing was continued further for 7 hours. The solvent portion reduced so that only half of the volume remains. The compound with crystalline form was separated on cooling. The collected compound was filtered and dried. The purification was done to obtain a pure product [24-25].

Similarly, **4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl) pyrimidin-2-amines (Va-k)** were synthesized.

Vb: Yellow solid, yield 65%, m.p-82-84 $^{\circ}$; IR (KBr): 3321, 3192, 1631, 1548, 1440, 1222, 765 cm^{-1} ; 1H NMR($CDCl_3$, 400 MHz): δ 2.44 (s, 3H, CH_3), 2.76 (s, 3H, CH_3), 4.63 (d, 2H, aromatic C-NH), 5.36 (s, 1H, NH-benzimidazole), 7.11 (s, 1H, 2-Pyrimidine) 7.49-7.69 (m, 3H, Benzimidazole), 7.91-8.43 (m, 4H, Quinoline). MS: m/z 400.80 ($M^{+\bullet}$).

Vd: Yellow solid, yield 60%, m.p. 84-86 $^{\circ}$; IR (KBr): 3404, 3182, 1651, 1531, 1456, 1222, 757 cm^{-1} ; 1H NMR($CDCl_3$, 400 MHz): δ 2.42 (s, 3H, CH_3), 2.67 (s, 3H, CH_3), 4.63 (d, 2H, aromatic C-NH), 5.46 (s, 1H, NH-benzimidazole), 7.07 (s, 1H, 2-Pyrimidine) 7.50-7.96 (m, 3H, Benzimidazole), 8.03-8.62 (m, 4H, Quinoline). MS: m/z 400.82 ($M^{+\bullet}$).

Vf: Yellow solid, yield 58%, m.p. 85-87 $^{\circ}$; IR(KBr): 3338, 3190, 1624, 1500, 1438, 1226, 775 cm^{-1} ; 1H NMR($CDCl_3$, 400 MHz): δ 2.47 (s, 3H, CH_3), 3.92 (s, 3H, OCH_3), 4.56 (d, 2H, aromatic C-NH), 5.29 (s, 1H, NH-benzimidazole), 7.01 (d, 1H, 2-Pyrimidine) 7.19-7.57 (m, 3H, Benzimidazole), 7.66-8.65 (m, 4H, Quinoline). MS: m/z 416.81 ($M^{+\bullet}$).

Vh : Yellow solid, yield 52%, m.p. 89-91°C; IR (KBr): 3630, 3450, 1647, 1502, 1442, 1224, 804, 825 cm^{-1} ; ^1H NMR(CDCl_3 , 400 MHz): δ 2.43 (s, 3H, CH_3), 4.62 (d, 2H, aromatic C-NH), 5.49 (s, 1H, NH-benzimidazole), 7.08 (d, 1H, 2-Pyrimidine) 7.45-7.74 (m, 3H, Benzimidazole), 7.86-8.78 (m, 4H, Quinoline). MS: m/z 422.20 ($\text{M}^+ + 1$).

Table 1 :Physical Characterization of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl) pyrimidin-2-amines (Va-k)

Sl. No	Compound Code	R	Molecular Formula	Molecular Weight	M.P $^{\circ}$
1	Va	H	$\text{C}_{21}\text{H}_{15}\text{ClN}_6$	386.83	79
2	Vb	6- CH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6$	400.86	82
3	Vc	7- CH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6$	400.86	80
4	Vd	8- CH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6$	400.86	84
5	Ve	6- OCH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6\text{O}$	416.86	87
6	Vf	7- OCH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6\text{O}$	416.86	85
7	Vg	8- OCH_3	$\text{C}_{22}\text{H}_{17}\text{ClN}_6\text{O}$	416.86	83
8	Vh	6-Cl	$\text{C}_{21}\text{H}_{14}\text{Cl}_2\text{N}_6$	421.28	89
9	Vi	7-Cl	$\text{C}_{21}\text{H}_{14}\text{Cl}_2\text{N}_6$	421.28	88
10	Vj	6-Br	$\text{C}_{21}\text{H}_{14}\text{BrClN}_6$	465.73	92
11	Vk	6-F	$\text{C}_{21}\text{H}_{14}\text{FCIN}_6$	404.82	86

Anthelmintic activity

The synthesized compounds were tested for anthelmintic activity by in-vitro bioassay method [26-28].

The south Indian adult earth worms *Pheretima posthuma* (earthworms authenticated by the Government Agricultural College, Hitnalli, Vijayapur, Karnataka) of 9-11cm in length and 0.2-0.3 cm in width were used for the in vitro anthelmintic bio-assay due to its anatomical and physiological resemblance with the intestinal worm parasites of human beings. Worms of almost equal size (9 ± 1 cm) were randomly selected for washing well with normal saline solution to remove all fecal and adherent materials before being released into petridishes containing drug in 15 ml of normal saline solution.

The worms were divided into the control, standard and tested groups of five earthworms in each group. All the tested compounds and the standard drug solution were freshly prepared before commencement of the experiments. The control group petridish contains 0.5ml of dimethylsulphoxide in 14.5ml of normal saline solution. The standard drug Albendazole and tested compounds were prepared at a doses level of 30, 50, 100 $\mu\text{g}/\text{ml}$ by dissolving in minimum quantity, about 0.5ml of dimethylsulphoxide and the volume was diluted to 15 ml with normal saline, then poured into petridishes.

The five earth worms were placed in each petridishes at room temperature and time taken for the induction of complete paralysis and time taken for death of individual earthworms was noted. The time when the worms were motionless and not even used to receive normal saline was found to be the time of paralysis. The death time was ascertained by applying external stimuli unless placing the individual worms in warm water at 50°C which stimulate and induce movement of worms, if alive. The mean paralysis time and mean death time were calculated for each tested concentrations of the compounds.

Table 2: Anthelmintic activity of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl)pyrimidin-2-amines (Va-k)

Pyrazolines	Time taken for paralysis (P)			Time taken for Death (D)		
	30µg/ml	50µg/ml	100µg/ml	30µg/ml	50µg/ml	100µg/ml
Va	44.02	20.56	9.31	61.52	36.78	16.22
Vb	14.20	11.15	6.05	31.80	21.88	07.26
Vc	18.50	13.20	5.99	36.04	22.40	09.02
Vd	16.42	11.12	6.95	33.61	22.02	08.22
Ve	19.22	16.24	7.01	43.79	24.24	11.02
Vf	19.00	15.44	7.29	40.80	25.26	12.81
Vg	46.51	20.05	8.23	65.16	38.79	18.28
Vh	21.22	15.03	7.56	49.37	28.76	13.12
Vi	28.74	19.00	7.97	50.79	30.18	17.83
Vj	30.57	18.42	7.80	58.08	33.74	14.24
Vk	35.24	17.65	8.00	54.51	30.72	15.20
ALZ ^a	13.90	12.48	6.93	27.27	18.44	9.42
Control ^b	-	-	-	-	-	-

Each value represents the Mean (n=5).

^aStandard drug- Albendazole (ALZ)

^bControl- Normal Saline

RESULTS AND DISCUSSIONS:

All the newly synthesized 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1H-benzimidazol-2-yl) pyrimidin-2-amines (Va-k) were characterized by IR, ¹H NMR and Mass spectral studies. It was observed that while increasing the concentrations of compounds and albendazole significantly reduced the time taken for paralysis and death as well. Compounds Vb, Vc and Vd showed excellent potent action for time taken to paralysis and death when compared to the standard drug albendazole. The compounds Ve, Vf and Vh were also registered comparably potent activity to the above mentioned compounds. The compounds Vi, Vj and Vk were also displayed good anthelmintic activity but compounds Va and Vg possess comparably less potent than other tested compounds.

CONCLUSION:

A new series of compounds of 4-(2-chloroquinolin-3-yl)-6-(6-methyl-1*H*-benzimidazol-2-yl)pyrimidin-2-amines (Va-k) were synthesized. The synthesized compounds were also screened for anthelmintic activity. The results of anthelmintic testing revealed the compounds Vb, Vc and Vd have shown promising anthelmintic activity. Therefore, this work would be fruitful matrix for the development of novel class of anthelmintic agents.

ACKNOWLEDGEMENT:

The authors thank the Rajiv Gandhi University of Health Sciences, Bangalore for financial support and also the principal and management of the BLDEA's SSM College of Pharmacy and Research Center, Vijayapur, Karnataka for the provision of facilities.

REFERENCES:

1. Nofall ZM, Soliman EA, Abd el-karim SS, Elzahar MI, Srour AM, Sethumadhavan S et al. Novel benzimidazole derivatives as expected anticancer agents. *Acta Poloniae Pharmaceutica n Drug Research*. 2011; 68 (4): 519-534.
2. Joshi CK, Jain R, Dandia A and Sharma K. Synthesis of [1,2,4] triazino[4,3-a]benzimidazol-4(10H)-ones as antimicrobial agents. *Indian Journal of Chemistry*. 1989; 28 (B): 698-701.
3. Shivakumar B, Anil Kumar KK, Madawali IM, Hugar S and Kalyane NV. Synthesis and antioxidant activity of new pyrazoles of 6-methylbenzimidazoles. *World Journal of Pharmaceutical Research*. 2018; 7 (16): 1017-1028.
4. Pandey VK, Gupta VD and Tiwari DN. 1,2-disubstituted benzimidazoles as potential antiviral agents. *Indian Journal of Heterocyclic Chemistry*. 2005; 14: 217-220.
5. Kumar JR, jawahar J and pathak DP. Synthesis of benzimidazole derivatives: as anti-hypertensive agents. *E-Journal of chemistry*. 2006; 3 (4): 278-285.
6. Valdez J, Cedillo R, Hernandez-Campos A, Yopez LN, Hernandez-Luis F, Navarrete-Vazquez G et al. Synthesis and antiparasitic activity of 1*H*-benzimidazole derivatives. *Bioorganic and Medicinal Chemistry Letters*. 2002; 12: 2221-2224.
7. Narayan reddy A, Patnaik S, Kalyane N and Reddy VM. Synthesis of some substituted imidazolino-[3,4-a]-2,3-dihydroimidazoles/benzimidazoles as possible nonsteroidal, non-acidic anti-inflammatory agents. *Indian Journal of Heterocyclic Chemistry*. 2003; 12:347-350.

8. Divakar KJ, Rao MK, Shrivastava R and Reddy AB. Synthesis and antifilarial activity of benzimidazole-2-carbamates carrying an amino acid side chain at the 5(6)-position. *Indian Journal of Chemistry*. 1989; 28(B): 252-260.
9. Sharma V and Sharma KV. Synthesis and biological activity of some 2-amino-4,6-substituted-diarylpyrimidines: reaction of substituted chalcones with guanidinium carbonate. *Rasayan Journal of Chemistry*. 2011; 4 (1): 17-23.
10. Bhargat CM and Ramesh B. Synthesis, antimicrobial screening and structure–activity relationship of novel pyrimidines and their thioethers. *Bulletin of Faculty of Pharmacy, Cairo University*. 2014; 52: 259–267.
11. Lingala S, Nerella R, Sambasiva Rao KRS. Synthesis, antimicrobial and anthelmintic activity of some novel benzimidazole derivatives. *Der Pharma Chemica*, 2011; 3 (4): 344-352.
12. Reddy VM and Reddy KR. Synthesis and biological evaluation of some novel-3-(5-substituted benzimidazol-2-yl)-5-arylisoxazolines. *Chinese Chemical Letters*. 2010; 21: 1145-1148.
13. Wang Z. Phillips-Ladenburg Benzimidazole Synthesis, In: *Comprehensive Organic Name Reactions and Reagents*. 2010; 496: 2197-2199.
14. Sharmila AG, Shivakumar B and Gaviraj EN. Synthesis and evaluation of new pyrazolines of benzimidazole as potent analgesic and anti inflammatory agents. *Der Pharma Chemica*. 2016; 8 (5): 33-37.
15. Dubey PK, Ramaiah K, Grossert JS, Hooper DL, and Ramanatham J. Studies on synthesis of 2-acetylbenzimidazole and related benzimidazole derivatives. *Journal of Indian Chemical Society*. 1999; 76: 140-144.
16. Kumar PK and Dubey PK. Studies on preparation of 2-Acetylbenzimidazole. *Der Pharma Chemica*, 2012; 4 (3):1292-1295.
17. Dubey PK, Ramanatham J, Kumar R and Kumar RC. Studies on synthesis of 1-alkyl/aryl-2-cinnamoylbenzimidazoles. *Indian Journal of Heterocyclic Chemistry*. 2000; 9: 259-262.
18. Singh RM and Srivastava A. Vilsmeier-Haack reagent: A facile synthesis of 2-chloro-3-formylquinolines from N-arylacetamides and transformation into different functionalities. *Indian Journal of Chemistry*. 2005; 44 (B): 1868-1875.
19. Ali MM, Sana SA, Tasneem, Rajanna KC and Saiprakash PK. Ultrasonically accelerated vilsmeier hack cyclisation and formylation reactions. *Synthitic communications*. 2002; 32(9): 1351-1356.

20. Rajakumar P and Raja R. Synthesis and photo physical properties of chiral dendrimers with quinoline surface group via click chemistry Tetrahedron Letters. 2010; 51: 4365-4370.
21. Tabassum S, Kumara THS, Jasinski JP, Millikan SN, Yathirajan HS, Ganapathy PS S. et al. Synthesis, crystal structure, ABTS radical-scavenging activity, antimicrobial and docking studies of some novel quino line derivatives. Journal of Molecular Structure. 2014; 1070: 10-20.
22. Ramesh E, Sree Vidhya TK and Raghunathan R. Indium chloride/silica gel supported synthesis of pyrano/thiopyranoquino lines through intramolecular imino Diels–Alder reaction using microwave irradiation. Tetrahedron Letters. 2008; 49: 2810-2814.
23. Nyerges M, Pinter A, Viranyi A, Blasko G and Toke L. Synthesis of pyrrolo[3,4-c]quinolines by 1,5-electrocyclisation of non-stabilised azomethine ylides. Tetrahedron. 2005; 61: 8199-8205.
24. Sawhney SN, Vir D and Gupta A. Synthesis and anti-inflammatory activity of some 2-(5-aryl-4,5-dihydropyrazol-3-yl)- and 2-(2-amino-6-arylpyrimidine-4-yl)benzimidazoles. Indian. Journal of Chemistry. 1990; 29 (B): 1107-1112.
25. Hussain KF, Ashwa A and Verma BL. Synthesis and reactions of 2-amino-4,6-diaryl pyrimidine derivatives. Asian Journal of Chemistry. 1997; 9 (1): 86-90.
26. Babu S and Selvakumar S. Synthesis and spectral characterization of some 2-[(1-((substituted phenylamino) methyl)-1-benzoimidazol-2-yl) alkyl] isoindoline-1,3-diones for in-vitro anthelmintic screening. Der Pharma Chemica. 2013; 5 (4):198-206.
27. Sreena K, Ratheesh R, Rachana M, Poornima M and Shyni C. Synthesis and anthelmintic activity of benzimidazole derivatives. Hygeia. 2009; 1 (1): 21-22.
28. Shahare MB, Kadam VJ, Jagdale DM, Gandhi PS and Gaikwad PI. Synthesis and evaluation of novel anthelmintic benzimidazole derivatives. International Journal of Research in Pharmacy and Chemistry. 2012; 2(1): 132-136.

AJPTR is

- Peer-reviewed
- bimonthly
- Rapid publication

Submit your manuscript at: editor@ajptr.com

