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Research Article

DESIGN, SYNTHESIS AND MOLECULAR DOCKING STUDIES OF NOVEL N-SUBSTITUTED-2-(FURAN-3-YL)-1*H*-BENZIMIDAZOLE DERIVATIVES

K. Srikanth Kumar[1]*, A. Lakshmana Rao[1], S. Ravichandra[2], A.N.V.S. Divya[1], Ch. Archana[1], A. Lavanya[1], A.V.D.S. Mani Kumar[1]

*[1]Department of Pharmaceutical Chemistry, V.V. Institute of Pharmaceutical Sciences, Gudlavalleru, [2]Department of Pharmaceutical Chemistry, Hindu College of Pharmacy, Guntur, India.

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Benzimidazole derivatives, synthesis, characterization, molecular docking, β-tubulin.

ABSTRACT

Benzimidazole pharmacophore possess broad class of curative properties like anthelmintic, antiulcer, antihypertensive, anticancer, etc. In view of this reason benzimidazole derivatives synthesis gained vital significance in recent years. In this investigation, a series of novel substituted benzimidazole derivatives having furan appendage at 2nd position and alkyl/aryl appendage at 1st position were synthesized by using appropriate procedures. All the compounds synthesized were characterized by physically (R_f values, Melting point, Molecular weight, Molecular formula) and were characterized by spectral data (^{1}H-NMR, ^{13}C-NMR, IR and Mass spectra). All the synthesized compounds were screened for molecular docking studies on human gamma-tubulin protein to find out the binding interaction at the target active site. Molecular docking studies at human gamma-tubulin protein states that the compound 4b showed good binding affinity (-8.98 kcal/mol) in comparison to the reference compound Albendazole (-8.47 kcal/mol).

INTRODUCTION

In the current drug discovery research, heterocyclic ring containing drug molecules gained much more importance. Heterocyclic compounds take over various fields such as organic chemistry, medicinal chemistry, biochemistry, agricultural sciences. Heterocyclic compounds chemistry played a fundamental role in the metabolism of most of all living cells[1]. Among different classes of heterocyclic compounds, benzimidazole is the key scaffold which can be found in many active pharmaceutical ingredients. The benzimidazoles contain a phenyl ring fused to an imidazole ring, as indicated in the structure for benzimidazole. Currently used antiulcer drugs- Omeprazole, Lansoprazole, Pantoprazole, Rabeprazole; anthelmintic drugs- Albendazole, Mebendazole, Thiabendazole possessing benzimidazole moiety were mentioned (Fig. 1).

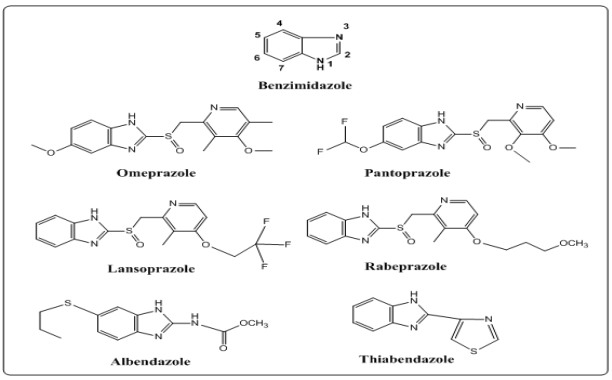
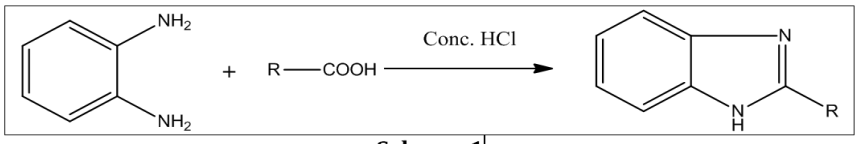


Fig. 1: Commonly used benzimidazole pharmacophore containing drugs

Benzimidazole nucleus containing compounds or derivatives possess broad range of therapeutic activities like anthelmintic, antiviral, antiulcer, antihypertensive, anticancer, etc. In recent years benzimidazole derivatives gained much more importance in organic synthesis[2,3]. Diverse synthetic approaches were reported in the literature for benzimidazole ring synthesis. *o*-phenylenediamine was condensed with various aldehydes using solid-supported catalyst[4], transition metal catalysts like $Sc(OTf)_3$[5], $Yb(OTf)_3$[6], $FeCl_3.6H_2O$[7], $In(OTf)_3$[8], Cobalt complexes[9] and also in the presence of different oxidizing agents like air[10], $Pb(OAc)_4$[11], Sulphamic acid[12], MnO_2[13], Oxone[14], Iodine[15], H_2O_2–HCl[16], DDQ[17] etc. Other approach states carboxylic acids condensed with *o*-phenylenediamine in the presence of acid catalysts[18].

Pharmaceutical, veterinary and agrochemical products developed with benzimidazole moiety includes Albendazole, mebendazole, thiabendazole, astemizole, lansoprazole, omeprazole, pantoprazole, etc[9]. Phillip's method[20], involves in the condensation of *o*-phenylenediamine with carboxylic acids or its derivatives, including heating the reagents together in the presence of concentrated HCL (Scheme 1), is the most common synthetic method for preparation of a wide range of benzimidazoles.



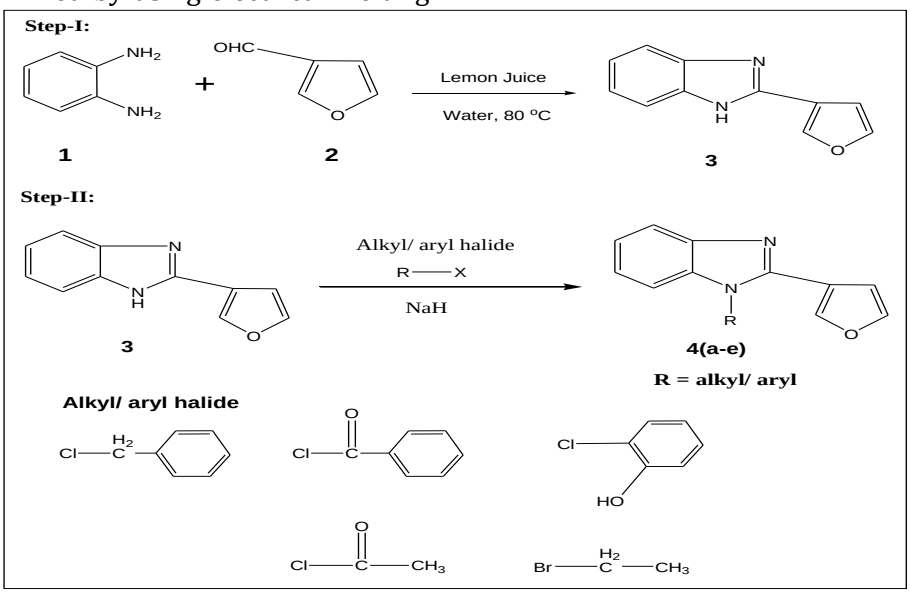
Scheme 1

In the present work a series of novel substituted benzimidazole derivatives having furan appendage at 2nd position and alkyl/aryl appendage at 1st position were synthesized by using appropriate procedures. All the synthesized compounds were characterised and tested for molecular docking studies.

MATERIALS AND METHODS

All the chemicals and reagents for the synthesis of N-substituted-2-(furan-3-yl)-1*H*-benzimidazole derivatives were procured from commercial suppliers of Merck grade. Completion of the reaction was monitored by thin layer chromatography with the help of E.Merck grade precoated silica gel 60-GF-254 TLC plates. Melting points were determined by using electrical melting point apparatus and those were uncorrected. By using KBr pressed pellet technique, IR spectra of the compounds were recorded in Bruker FT-IR analyzer spectrophotometer. Chemical shifts in ppm of ^{1}H-NMR spectra and ^{13}C-NMR were recorded on Bruker-AMX-400MHz spectrophotometer using deuterated dimethyl sulfoxide (DMSO) solvent and tetramethylsilane (TMS) as internal standard. Mass spectra of the compounds were recorded on an Agilent LC-MSD-1200 mass spectrometer. All the novel synthesized compounds were evaluated for molecular docking studies on β-tubulin protein to find out the binding interaction at the target site.

EXPERIMENTAL



Scheme 2: Scheme of synthesis of N-substituted-2-(furan-3-yl)-1*H*-benzimidazoles

Lemon Juice Preparation[21]

Lemon botanically *Citrus limonium*, *Citrus aurantium* and *Citrus indica* are the species of citrus family. Presence of citric acid and ascorbic acids in lemon juice acts as acid catalyst in organic reactions. Fresh lemons were purchased, obtained the juice by making them into pieces and with the help of juicer. Juice was further filtered through filter paper and clear solution of juice was used as reaction catalyst. The pH of the extracted lemon juice was found to be 2.4.

Step-I: Procedure for Synthesis of 2-(furan-3-yl)-1*H*-benzimidazole (3)[21]

To a mixture of *o*-phenylenediamine (0.02 mol) and furfural (0.02 mol) add 6-8ml of 1:1 V/V lemon juice: water mixture. The reaction mixture was refluxed for 3-4 hrs at 80°C. The completion of the reaction was confirmed by TLC (using Silica Gel - G stationary phase and ethylacetate:hexane, 1:2 V/V as mobile phase). The reaction mixture was quenched with cold water and stirred continuously until free flowing solid was obtained. The resulting solid was filtered, air dried and purified by recrystallization from 95% ethanol to get pure product.

Step-II: Procedure for synthesis of N-substituted-2-(furan-3-yl)-1*H*-benzimidazole (4a-4e)[22]

To a mixture of 2-(furan-3-yl)-1*H*-benzimidazole **(*3*)** (0.02 mol) and alkyl/aryl halide (0.02 mol) in 10ml of THF, little quantity of sodium hydride (2 g) was added. The resulting mixture was stirred for 8-12 hrs at 40-50°C. The completion of the reaction was confirmed by TLC (using Silica Gel - G stationary phase and ethylacetate: hexane, 1:2 V/V as mobile phase). Excess solvent was removed by distillation. The crude product was washed with cold water, extracted with ethyl acetate and finally purified by recrystallization from 95% ethanol to get pure product.

Spectral Data

N-benzyl-2-(furan-3-yl)-1*H*-benzimidazole (4a): IR [KBr, cm^{-1}]: 3064.24 (=CH stretch), 2963.18 (-CH stretch), 1628.46 (C=N stretch), 1567.18 (C=C stretch), 1329.09 (C-N stretch), 1094.33 (C-O stretch). ^{1}H-NMR (400 MHz, DMSO-D_6) δ: 7.914 (1H, s, Furan C_2-H), 6.845-7.017 (1H, d, Furan C_4-H), 7.215-7.321 (1H, d, Furan C_5-H), 7.339-7.505 (5H, m, Phenyl), 7.611-7.698 (2H, dd, benzimidazole C_5-H & C_6-H), 7.892-7.917 (2H, dd, benzimidazole C_4-H & C_7-H), 5.523 (2H, s, -C$\underline{H}_2$-phenyl). ^{13}C-NMR (100 MHz, DMSO-D_6) δ: 158.65, 146.65, 143.97, 138.64, 136.31, 133.08, 129.07, 128.11, 125.47, 124.74, 122.88, 119.34, 117.36, 107.37, 53.48. ESI-MS: m/z (M^+) 274.

N-benzoyl-2-(furan-3-yl)-1*H*-benzimidazole (4b): IR [KBr, cm^{-1}]: 3019.88 (=CH stretch), 1709.44 (C=O stretch), 1633.94 (C=N stretch), 1555.72 (C=C stretch), 1309.65 (C-N stretch), 1086.12 (C-O stretch). ^{1}H-NMR (400 MHz, DMSO-D_6) δ: 6.882-7.200 (1H, d, Furan C_4-H), 7.219-7.478 (5H, m, Phenyl), 7.506-7.526 (2H, dd, benzimidazole C_5-H & C_6-H), 7.742-7.747 (1H, d, Furan C_5-H), 7.880-7.899 (2H, dd, benzimidazole C_4-H & C_7-H), 8.069 (1H, s, Furan C_2-H). ^{13}C-NMR (100 MHz, DMSO-D_6) δ: 165.73, 145.35, 140.21, 138.71, 136.54, 134.11, 133.08, 131.92, 130.31, 128.64, 126.45, 123.10, 116.76, 113.28, 108.59. ESI-MS: m/z (M^+) 288.

N-(*o*-hydroxyphenyl)-2-(furan-3-yl)-1*H*-benzimidazole (4c): IR [KBr, cm^{-1}]: 3423.29 (OH stretch), 3070.51 (=CH stretch), 1608.26 (C=N stretch), 1528.80 (C=C stretch), 1318.47 (C-N stretch), 1079.09 (C-O stretch). ^{1}H-NMR (400 MHz, DMSO-D_6) δ: 6.860-7.127 (1H, d, Furan C_4-H), 7.239-7.280 (4H, m, Phenyl), 7.511-7.539 (2H, dd, benzimidazole C_5-H & C_6-H), 7.746-7.767 (1H, d, Furan C_5-H), 7.886-7.900 (2H, dd, benzimidazole C_4-H & C_7-H), 8.095 (1H, s, Furan C_2-H), 5.323 (1H, s, OH). ^{13}C-NMR (100 MHz, DMSO-D_6) δ: 149.26, 146.32, 143.18, 141.08, 138.64, 135.19, 129.71, 127.84, 126.33, 124.55, 122.07, 120.38, 118.47, 115.81, 112.42, 107.66. ESI-MS: m/z (M^+) 276.

N-acetyl-2-(furan-3-yl)-1*H*-benzimidazole (4d): IR [KBr, cm^{-1}]: 3044.35 (=CH stretch), 2966.25 (-CH stretch), 1715.08 (C=O stretch), 1624.22 (C=N stretch), 1549.64 (C=C stretch), 1333.60 (C-N stretch), 1077.15 (C-O stretch). ^{1}H-NMR (400 MHz, DMSO-D_6) δ: 7.708 (1H, s, Furan C_2-H), 6.964-7.108 (1H, d, Furan C_4-H), 7.402-7.499 (1H, d, Furan C_5-H), 7.227-7.318 (2H, dd, benzimidazole C_5-H & C_6-H), 7.542-7.609 (2H, dd, benzimidazole C_4-H & C_7-H), 2.548 (3H, s, -COC$\underline{H}_3$). ^{13}C-NMR (100 MHz, DMSO-D_6) δ: 167.29, 145.19, 142.37, 138.26, 135.97, 133.47, 128.47, 124.08, 116.37, 113.48, 108.72, 23.67. ESI-MS: m/z (M^+) 226.

N-ethyl-2-(furan-3-yl)-1*H*-benzimidazole (4e): IR [KBr, cm^{-1}]: 3056.97 (=CH stretch), 2989.27 (-CH stretch), 1633.83 (C=N stretch), 1569.55 (C=C stretch), 1348.73 (C-N stretch), 1081.86 (C-O stretch). ^{1}H-NMR (400 MHz, DMSO-D_6) δ: 7.816 (1H, s, Furan C_2-H), 6.817-6.907 (1H, d, Furan C_4-H), 7.195-7.207 (1H, d, Furan C_5-H), 7.310-7.399 (2H, dd, benzimidazole C_5-H & C_6-H), 7.566-7.611 (2H, dd, benzimidazole C_4-H & C_7-H), 4.156-4.408 (2H, q, -C$\underline{H}_2$CH$_3$), 1.391-1.529 (3H, t, -CH$_2$C$\underline{H}_3$). ^{13}C-NMR (100 MHz, DMSO-D_6) δ: 156.09, 145.31, 141.20,

137.97, 134.75, 129.46, 125.34, 119.66, 112.28, 107.36, 41.67, 18.71. ESI-MS: m/z (M^+) 212.

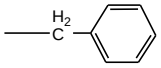
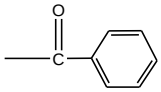
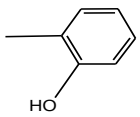
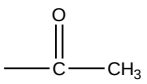
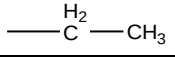
Molecular docking studies

Molecular docking studies on human gamma tubulin protein[23]. The ligand molecules were designed, and the structures were analyzed by using ChemDraw Ultra 12.0. Three-dimensional (3D) structure coordinates were prepared using Chem3D ultra 12.0. Nonpolar hydrogen atoms were merged, and the rotatable bonds were set by using Auto-Dock 4.2 Tools. The crystal structure of human gamma-tubulin (PDB ID: 1Z5V) was selected from the PDB (www.rcsb.org/pdb) and was edited by removing the heteroatoms, adding C terminal oxygen. Polar hydrogens and Gasteiger charges were added after merging non-polar hydrogens. The grid map was centered at the active pocket of the protein by AutoGrid4. It is the grid map, which was centered at the active pocket of the protein. Automated docking was used to determine the orientation of inhibitors bound in the active site. A Lamarckian genetic algorithm method, implemented in the program AutoDock 4.2, was employed to identify appropriate binding modes and conformations of the ligand. The Lamarckian genetic algorithm methods were applied for minimization, using default parameters. Binding energy, number of H-bonds, H-bond length and amino acid residues interacted were recorded in each ligand confirmations.

RESULTS AND DISCUSSION

N-substituted-2-(furan-3-yl)-1*H*-benzimidazole derivatives were synthesized using the appropriate synthetic procedure (Scheme 2) i.e. reaction of *o*-phenylenediamine (1) and furfural (2) in presence of lemon juice and water gives 2-(furan-3-yl)-1*H*-benzimidazole (3). Further the title compounds 1-substituted-2-substituted benzimidazole derivatives (4a-4e) were prepared by the reaction of 2-(furan-3-yl)-1*H*-benzimidazole (3) with different alkyl/ aryl halides in presence of sodium hydride using THF as solvent. The progress of the reaction was monitored by TLC. Finally, the reaction mixture was poured onto the crushed ice and then recrystallized from ethanol. Melting points were determined in open capillaries and were uncorrected. IR spectra of the compounds were recorded in KBr discs on Bruker FT-IR analyzer spectrophotometer. ^{1}H-NMR spectra were recorded on Bruker-400MHz spectrophotometer and ^{13}C-NMR spectra were recorded on Bruker-AMX-400MHz spectrophotometer. Mass spectra of the compounds were recorded on an Agilent LC-MSD-1200 mass spectrometer. Physical characterization data of all the synthesized compounds were given in Table I.

Table I: Physical characterization data of the synthesized compounds 4a-4e

Compd.	R	m.p. (ºC)	Molecular formula	m.w.	% yield	R_f value
4a		226-228	$C_{18}N_2H_{14}O$	274	79.48	0.54
4b		212-214	$C_{18}H_{12}N_2O_2$	288	70.86	0.61
4c		240-242	$C_{17}H_{12}N_2O_2$	276	80.26	0.65
4d		230-232	$C_{13}H_{10}N_2O_2$	226	75.47	0.58
4e		202-204	$C_{13}H_{12}N_2O$	212	73.58	0.51

The molecular docking of ligand molecules with human gamma-tubulin revealed that most of the molecules exhibited the bonding with one or the other amino acids in the active pockets. Theoretically all the ligand molecules showed encouraging binding energy. Among the five molecules, docking of human gamma-tubulin revealed that their binding energy were -6.89, -8.98, -8.66, -8.35 and -7.88 kcal/mol respectively. Molecules 4b and 4c showed significant binding affinity towards the active pocket with good binding energy, ligand efficiency and hydrogen bonding, those can be considered as good inhibitor of human gamma-tubulin. The binding energy values revealed that the compounds 4b and 4c showed good binding affinity towards the human gamma-tubulin and the computed values were depicted in the Table II. The interaction of Albendazole at the active site of the

human gamma-tubulin has showed binding energy of -8.47 kcal/mol and the amino acids interacted were Thr131, Gly132, Gly129, Val160, Ser126 and Cys12. The 3D structure of human gamma-tubulin, docking complex of human gamma-tubulin protein-1Z5V against Albendazole, compound 4b and compound 4c was shown in the Fig. 2. The compound 4b shown promising binding affinity i.e. -8.98 kcal/mol and the amino acids interacted were Phe208, Cys12, Ser126, Ala128, Val157, Pro159, Asn190.

Table II: **Binding energy and amino acid residues interacted by the compounds 4a-4e with the target β-tubulin protein PDB ID – 1Z5V**

Compound	Binding energy (kcal/mol)	No. of H bonds	H-bond length	Amino acid residues interacted
Albendazole	-8.47	8	2.04, 2.27, 2.19, 3.35, 2.35, 5.03, 4.93, 4.32	Thr131, Gly132, Gly129, Val160, Ser126, Cys12
4a	-6.89	5	3.16, 2.85, 4.31, 2.64, 3.68	Ala128, Gly132, Val157, Pro159, Ser126, Phe208
4b	-8.98	9	2.74, 2.77, 3.73, 1.90, 4.97, 4.30, 4.11, 3.18, 5.70	Phe208, Cys12, Ser126, Ala128, Val157, Pro159, Asn190
4c	-8.66	7	4.17, 2.68, 2.49, 3.85, 2.82, 4.81, 3.28	Glu62, Gly132, Gly130, Val164
4d	-8.35	7	3.62, 5.37, 3.61, 3.58, 3.90, 2.60, 2.84	Cys12, Val157, Phe208, Asn190
4e	-7.88	5	3.56, 2.41, 5.61, 4.22, 3.22	Val160, Gly131, Phe208, Pro159

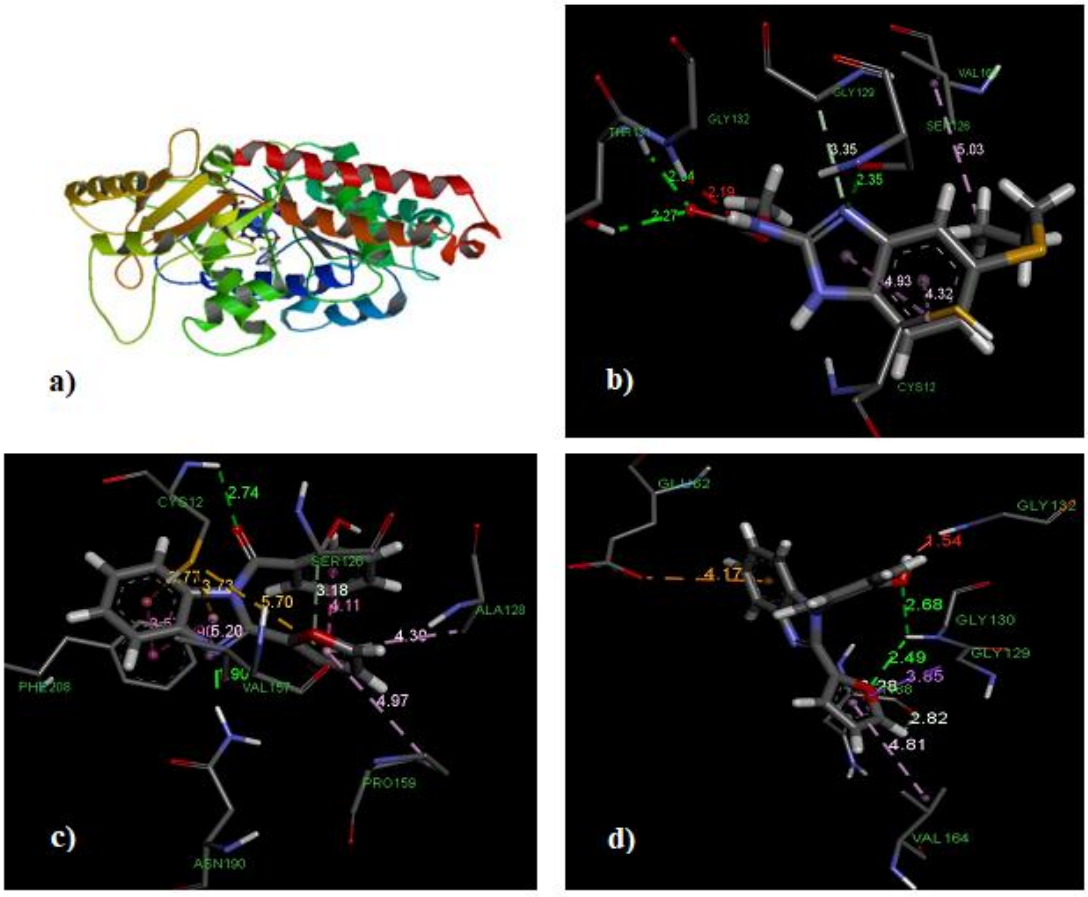


Fig. 2: **Molecular docking studies at β-tubulin protein (PDB ID- 1Z5V).**

a) Structure of β-tubulin protein PDB ID- 1Z5V.
b) Docking complex β-tubulin protein (PDB ID-1Z5V) with Albendazole.
c) Docking complex of β-tubulin protein (PDB ID-1Z5V) with compound 4b.
d) Docking complex of β-tubulin protein (PDB ID-1Z5V) with compound 4c

CONCLUSION

A facile method under mild conditions has been developed for the synthesis of the title compounds. In this investigation various novel benzimidazole derivatives (4a-4e) possessing furan appendage at 2nd position and alkyl/aryl appendage at 1st position were developed. Characterization of the compounds was done by physically and spectrally. Among the synthesized compounds N-(*o*-hydroxyphenyl)-2-(furan-3-yl)-1*H*-benzimidazole (4c) gives high percentage yield. Molecular docking studies at human gamma-tubulin protein states that the compound 4b and 4c showed good binding affinity (-8.98 & -8.66 kcal/mol) in comparison to the reference compound Albendazole (-8.47 kcal/mol).

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REFERENCES

1. Monika G. Heterocyclic Compounds and their Biological Significance: A Review. Int. J. Phys. Chem. Math. Sci. 2015; 4(1): 21-24.
2. Gravatt G.L., Baguley B.C., Wilson W.R., Denny W.A.: Synthesis and antitumor activity of DNA minor groove-targeted aniline mustard analogs of pibenzimol (Hoechst 33258). J. Med. Chem. 1994; 37(25): 4338-4345.
3. Srinivas U., Srinivas Ch., Narender P., Rao J., Palaniappan S.: Polyaniline-sulfate salt as an efficient and reusable catalyst for the synthesis of 1,5-benzodiazepines and 2-phenyl benzimidazoles. Catal. Commun. 2007; 8(1): 107-110.
4. Itoh T., Nagata K., Ishikawa H., Ohsawa A.: Synthesis of 2-arylbenzothiazoles and imidazoles using scandium triflate as a catalyst for both a ring closing and an oxidation steps. Heterocycles. 2004; 63(12): 2769-2783.
5. Massimo C., Francesco E., Francesca M.: Ytterbium triflate promoted synthesis of benzimidazole derivatives. Synlett. 2004; 10: 1832-1834.
6. Singh M.P., Sasmal S., Lu W., Chatterjee M.N.: Synthetic utility of catalytic Fe(III)/Fe(II) redox cycling towards fused heterocycles. A Facile access to substituted benzimidazole, bisbenzimidazole and imidazopyridine derivatives. Synthesis. 2000; 10: 1380-1390.
7. Trivedi R., De S.K., Gibbs R.A.: A convenient one-pot synthesis of 2-substituted benzimidazoles. J. Mol. Catal. A: Chem. 2006; 245(1-2): 8-11.
8. Chari M.A., Shobha D., Sasaki T.: Room temperature synthesis of benzimidazole derivatives using reusable cobalt hydroxide (ii) and cobalt oxide (ii) as efficient solid catalysts. Tetrahedron. Lett. 2011; 52(43): 5575-5580.
9. Lin S., Yang L.: A simple and efficient procedure for the synthesis of benzimidazoles using air as the oxidant. Tetrahedron. Lett. 2005; 46(25): 4315-4319.
10. Stephens F.F. and Bower J.D.: 626. The preparation of benziminazoles and benzoxazoles from Schiff's bases. Part I. J. Chem. Soc. 1949; 2971-2972.
11. Chakrabarty M., Karmakar S., Mukherji A., Arima S., Harigaya Y.: Application of sulfamic acid as an eco-friendly catalyst in an expedient synthesis of benzimidazoles. Heterocycles. 2006; 68(5): 967-974.
12. Bhatnagar I. and George M.V.: Oxidation with metal oxides—II: Oxidation of chalcone phenylhydrazones, pyrazolines, *o*-aminobenzylidine anils and *o*-hydroxy benzylidine anils with manganese dioxide. Tetrahedron. 1968; 24(3): 1293-1298.
13. Beaulieu P.L, Hache B., Von Moos E.: A practical oxone-mediated, high-throughput, solution-phase synthesis of benzimidazoles from 1,2-phenylenediamines and aldehydes and its application to preparative scale synthesis. Synthesis. 2003; 11: 1683-1692.
14. Gogoi P. and Konwar D.: An efficient and one-pot synthesis of imidazolines and benzimidazoles via anaerobic oxidation of carbon–nitrogen bonds in water. Tetrahedron. Lett. 2006; 47(1): 79-82.
15. Bahrami K., Khodaei M.M., Kavianinia I.: A simple and efficient one-pot synthesis of 2-substituted benzimidazoles. Synthesis. 2007; 4: 547-550.
16. Vanden Eynde J.J., Delfosse F., Lor P., Haverbeke Y.V.:2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, a mild catalyst for the formation of carbon-nitrogen bonds. Tetrahedron. 1995; 51(20): 5813-5818.
17. Middleton R.W.; Wibberley D.G.: Synthesis of imidazo[4,5-*b*] and [4,5-*c*]pyridines. J. Heterocycl. Chem. 1980; 17(8): 1757-1760.
18. Al-Muhaimeed H.: A parallel-group comparison of astemizole and loratadine for the treatment of perennial allergic rhinitis. J. Int. Med. Res. 1997; 25(4): 175–181.
19. Shatha I.A.: Synthetic approaches to benzimidazoles from *o*-phenylenediamine: A

literature review. J. Saudi Chem. Soc. 2017; 21(2): 229-237.

20. Phillip M.: J. Chem. Soc. 1971; 1143–1145.
21. Monika A.P., Panchsheela A.U., Shrikrishna S.K., Vasant B.H.: Lemon Juice: An Environmentally Benign Catalyst for Synthesis of Benzothiazoles and Benzoxazole Derivatives in Aqueous Medium. Der Chemica Sinica. 2017; 8(1): 198-205.
22. Ashish Kumar T. and Anil M.: Synthesis and antiviral activities of N-substituted-2-substituted-benzimidazole derivatives, Indian J. Chem. 2006: 45B: 489-493.
23. Samina N., Farzana L.A., Tajammul H., Kehkashan M., Ambreen G.M., Zaheer-ul-H.Q., Talat M., Humera N., Bushra M.: Brine shrimp lethality assay 'an effective prescreen': Microwave-assisted synthesis, BSL toxicity and 3DQSAR studies-based designing, docking and antitumor evaluation of potent chalcones. Pharm. Biol. 2013; 51(9): 1091–1103.

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***Address for correspondence**
Mr. K. Srikanth Kumar
Associate Professor,
V. V. Institute of Pharmaceutical Sciences, Gudlavalleru, Andhra Pradesh, India.
E-mail:karumanchi002@gmail.com
Contact No.: +91-9494682732