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SYNTHESIS DOCKING AND QSAR STUDIES OF QUINOLINE DERIVATIVES

B. Mayuri, N.Pramod*, R. Nagendra Babu, S.Chandra Prakash, R.J. Naveen Kumar, K. Madhuri

Department of Pharmaceutical Chemistry, Annamacharya College of Pharmacy Rajampet, Kadapa Dist. Andhra Pradesh, India.

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***Correspondence for Author**
Pramod Nayanapalli
Department of Pharmaceutical Chemistry, Annamacharya College of Pharmacy Rajampet, Kadapa Dist. Andhra Pradesh, India.

ABSTRACT

Five novel quinoline derivatives (BPM-1 to BPM-5) are synthesized. The synthetic scheme of quinolines derivative involves the reaction between 2-methoxy acetanilide with Vilsmayer Hack reagent ($POCl_3$, DMF).The formed 2-chloro-3-formyl-8-methoxy-quinolines. Further treated with sodium sulfide flakes resulted in to 3-formyl-8-methoxy 2-thio quinolines. Finally fused with various aryl amines to give 5-novel quinoline derivatives. Docking and Qsar studies where performed for designed compounds using Autodock 4.2 version. The results of Docking and Qsar studies reveled that both compounds BPM-1 and BPM-2 possess similar antibacterial activity.

KEYWORDS: Quinoline derivatives, Docking, QSAR, antibacterial activities.

INTRODUCTION

Quinoline is a heterocyclic compound in which benzene fused with pyridine. Quinoline was first isolated from coal tar in 1834. Shortly after the isolation of quinoline from coal tar it was also recognized as a pyrolytic degradation product of Cinchonamine, an alkaloid closely related to quinine, from which the name quinoline is derived; the word quinine, in turn, derives from *quina*, a Spanish version of a local South American name for the bark of quinine-containing *Cinchona* species.

The chemistry of quinoline derivatives has been of increasing interest since many of these compounds have been found useful as chemotherapeutic agents against malaria parasite all

the anti-malarial agents have a quinoline ring or a quinoline with an additional benzene added (an acridine rings) as a common structural features.[1-4]

Quinoline derivatives are pharmaceutically interesting compounds and many of them have been registered as drugs. Quinoline compounds can possess analgesic, anti-inflammatory, anti-malarial, anti-neoplastic, anti-leishmanial, immuno-modulator, anti-convulsant, anti-fungal, anti-bacterial, neurotropic, vasorelaxing and anti-viral activities.[5-8]

A volumetric representation of chosen binding cavity is approximately by using of set of various sizes which are mathematically placed in the distance between the carrier of spreads as a compare to representation of shape of cavity.

Quantitative structure activity relationship(QSAR)is possible to elustrte the influence of various physic chemical property on the drug potency and predict the activity of compounds with in a limits.

MATERIALS AND METHODS

All chemicals used were of analytical grade and purchased from SD Fine. Melting points of all the synthesized compounds were determined by open capillary tube method. The purity of all compounds was checked by TLC technique and spots were visualized using UV radiation/iodine chamber. Docking were performed by Autodock 4.2 version.

EXPERIMENTAL WORK

The synthesis of title compound has been affected as indicated in **Scheme-I.**

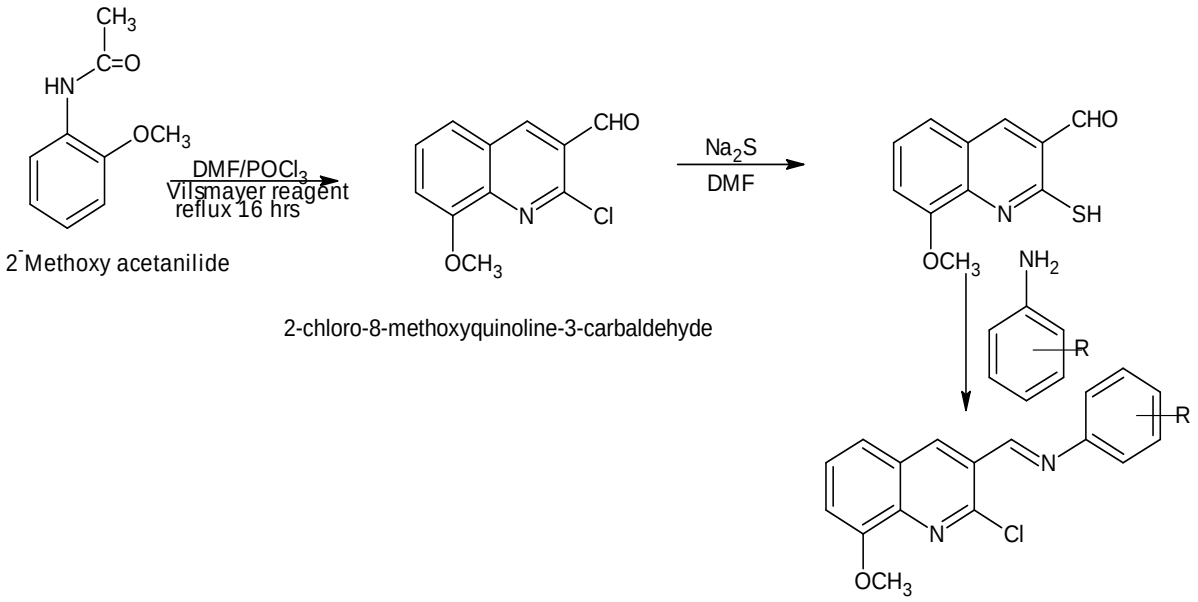


Table 1: Docking results of BPM1 and BPM2 compounds targeting ATP binding pocket of Beta-lactam enzyme towards anti-bacterial activity in specific to cell wall formation inhibition

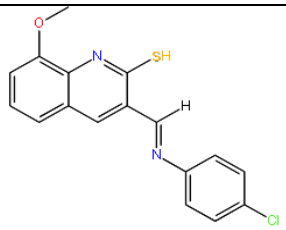
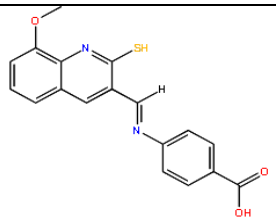
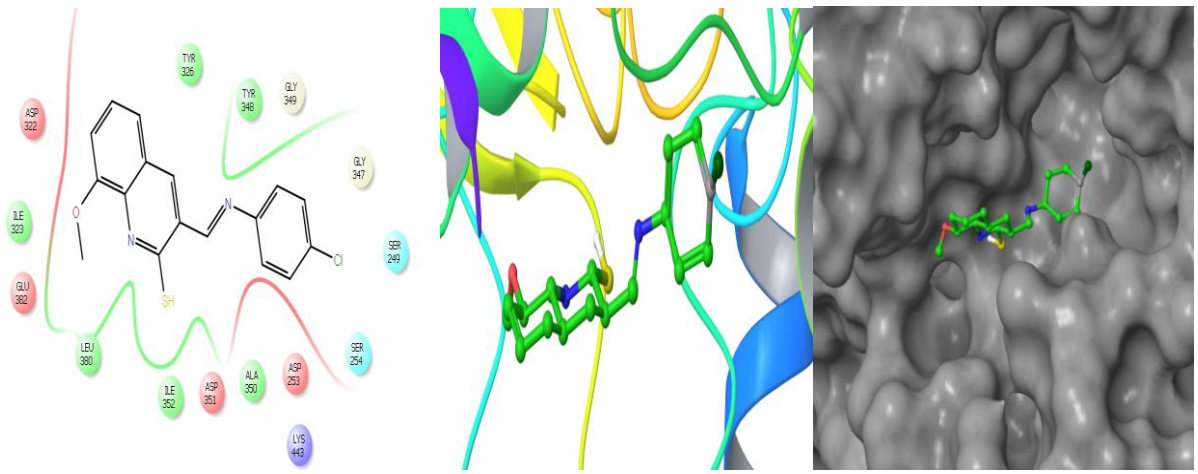
S. No.	Drug target	Compound Name	Compound Structure	Binding Energy in Kcal/mol	Predicted IC50 value
1.	ATP binding pocket of Beta-lactam	BPM1		-9.4	127.82 (nano molar)
2.		BPM2		-9.4	127.7 (nano molar)

Table 2: QSAR molecular descriptor values of the compounds BPM1 and BPM2 for ADME predictions according to Lipinski's rule of five.

S.No	Compound name	Molecular Formula	Mol. wt.	Log P	No. of H-bond donors	No. of H-bond acceptors	No. of rotatable bonds	TPSA	ADME pass/fail
1.	BPM1	$C_{17}H_{13}CLN_2OS$	328.824	4.825	0	3	3	34.49	PASS
2.	BPM2	$C_{18}H_{14}N_2O_3S$	338.388	4.058	1	5	4	71.789	PASS

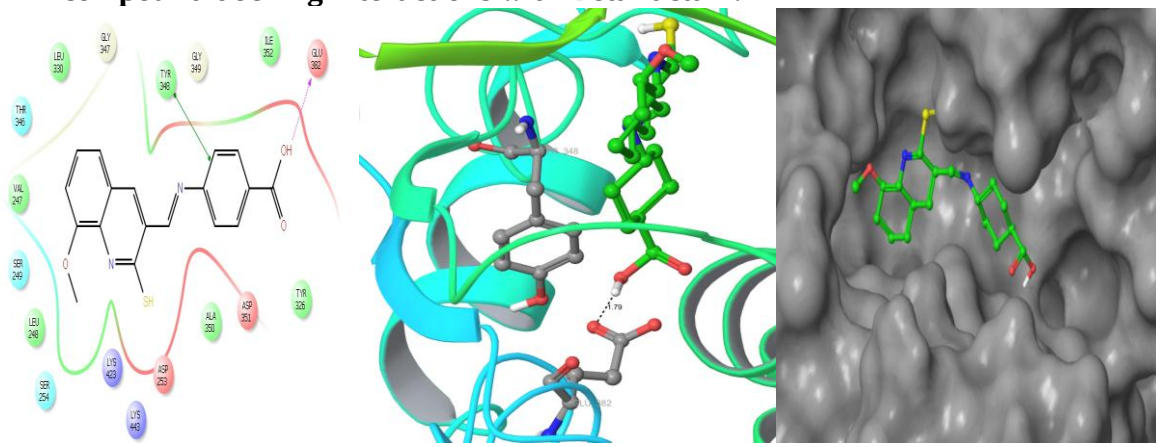
BPM1compound docking interactions with Beta-lactam.



(A) (B (C)

Figure 1: a) represents 2D interactions of compound BPM1, b) represents 3D interaction formed by the compound BPM1 (No H-Bonds formed), whereas c) represents Surface area interactions of compound BPM1.

BPM2 compound docking interactions with Beta-lactam.



(A) (B) (C)

Figure 2: a) represents 2D interactions of compound BPM2, b) represents 3D H-bond interaction formed by the compound BPM2, whereas c) represents Surface area interactions of compound BPM2.

CONCLUSION

Five novel quinoline derivatives were synthesized, characterized by IR spectroscopy, docking QSAR studies were performed for the designed compounds. For BPM-1 and BPM- 2 DOKING and QSAR studies revealed that the target site for anti-bacterial activity is ATP pocket of betalactam site and BPM-1 and BPM- 2 contains similar IC 50 values, it indicates that there is no much change in activity with respective to change in functional group. From theQSAR values for BPM 1&2 then log values TPA(total polar surface area)are similar also.

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