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Evaluation of in vitro and in-silico anti-bacterial activities of novel para substituted methoxy and chloro derivatives of quinazolinone

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Among the plethora of microorganisms encountered daily, some exhibit pathogenic qualities while others offer benefits. The ongoing battle against pathogenic microorganisms escalates considering increasing antibiotic resistance, prompting the need for novel strategies to impede or eradicate these entities. A main approach in the realm of antimicrobial tactics involves targeting DNA gyrase, a protein pivotal for processes such as replication, repair, and growth. Among the vast range of existing anti-bacterial drugs Quinazolinone based compounds are much prominent. This research focused on the synthesis of novel 6-bromo-2-phenylquinazolin-4(*3H*)-one, 6-bromo-2-(4-methoxyphenyl)quinazolin-4(*3H*)-one and 6-bromo-2-(4-chlorophenyl)quinazolin-4(*3H*)-one and the evaluation of their anti-microbial activities against *Escherichia coli* (ATCC 25921). The selection of functional groups for the derivatives, based on their electron-withdrawing and donating properties, was geared towards augmenting antimicrobial efficacy by impeding crucial processes like cell wall formation and replication. The structures of the synthesized analogues were confirmed using spectroscopic techniques such as FT-IR, ^{1}H NMR, ^{13}C NMR, High Resolution Mass Spectroscopy and by determining the melting points of the compounds. *In-silico* investigations utilizing molecular docking strategies done through auto dock vina have unveiled encouraging findings, showcasing strong binding affinities with DNA gyrase of *E.coli*. Both 6-bromo-2-(4-methoxyphenyl)quinazolin-4(*3H*)-one and 6-bromo-2-(4-chlorophenyl)quinazolin-4(*3H*)-one compounds and the standard ciprofloxacin gave binding affinities higher than -7.0 kcal/mol indicating their higher interactions with DNA gyrase in inhibition of cell wall synthesis of the micro-organism. However, the synthesized compounds failed to demonstrate noteworthy antimicrobial efficacy against *E.coli* in the well diffusion test, contrary to the favourable molecular docking results. The para substituted compounds 6-bromo-2-(4-methoxyphenyl)quinazolin-4(*3H*)-one and 6-bromo-2-(4-chlorophenyl)quinazolin-4(*3H*)-one showed positive activity (maximum zone of inhibition values of 15.0 ± 1.00 mm and 13.0 ± 0.58 mm respectively) compared to the 6-bromo-2-phenylquinazolin-4(*3H*)-one showcasing that electron donating or electron withdrawing effects at para position showed no considerable difference, concluding that para position substitution may enhance the anti-bacterial activity of the compound. Hence this study demonstrates the easy synthesis of 6th position brominated 2-phenyl-*3H*-quinazolin-4-one derivatives through oxidative cyclocondensation of 2-amino-5-bromobenzamide with an aryl aldehyde and determination of their antibacterial activities showcasing the need of further modifications and accurate methods for in-silico and in-vitro evaluations.

Keywords: Anti-microbial, Binding affinities, I*n-silico*, Well diffusion