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Synthesis, antimicrobial activity and molecular docking of novel tetracyclic scaffolds incorporating a flavonoid framework with medium sized oxygen heterocycles

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A convenient approach for the synthesis of novel tetracyclic scaffolds incorporating a flavonoid framework with medium sized heterocyclic rings (eight-, nine-, ten- and eleven-membered rings) containing two oxygen atoms from flavonols through alkylation using different dibromoalkanes was described. The synthesized compounds were established based on the spectral data and X-ray crystal structure for **6c**. The synthesized compounds were evaluated for their *in vitro* antimicrobial activity. Docking studies were carried out for most active two compounds **6f** and **6i**.

Keywords: Flavonoid framework, Medium sized rings, Antimicrobial activity, Molecular docking

Medium sized heterocyclic rings are commonly found structural units within the frame work of a variety of natural products and is the main reason for the growing importance of such class of compounds.[1] In particular synthesis of medium sized heterocyclic rings bearing oxygen or nitrogen atom(s) are important synthetic targets for organic chemists as they are integral parts of many medicinally interesting synthetic compounds. However synthesis of medium sized heterocyclic rings continues to be one of the fascinating endeavours in organic chemistry because of challenges involved in their synthesis.[2] Moreover for an equal number of atoms, cyclic analogues inherently possess a lower number of rotatable bonds than their acyclic analogues. As a result cyclic counterparts are more conformationally restricted than their acyclic analogues, which potentially can impart higher target binding and selectivity and improved oral bioavailability.[3] Flavonoid framework is medicinally important structural organization present in many bioactive molecules showing various activities like antiviral, antibacterial, antiprotozoal, oestrogenic, anti-inflammatory, mutagenic, antimutagenic and antineoplastic activities, and is also capable of inhibiting many types of enzymes.[4-6] Therefore there has been increasing interest in the synthesis of diverse classes of compounds containing flavonoid frame work.

Among numerous known heterocycles containing flavonoid framework, artelastocarpin and carpelastofuran (Figure 1) have attractive frameworks because of their reported cytotoxic properties.[7]