ABSTRACT

Nature always stands as a golden mark to exemplify the outstanding phenomenon of symbiosis. Several herbs consist of powerful ingredients, which are helpful to cure a number of health problems. Semi-synthetic derivatives have huge scope of synthesizing compounds with very less toxicity and also provide more lead moieties, thus play a major role in drug discovery. In the present study, author has proposed to synthesize semi-synthetic compounds of commonly available flavonoids viz hesperidin and naringin.

A total of thirty eight semi-synthetic derivatives were synthesized. The compounds synthesized were subjected for thin layer chromatography to identify purity. The synthesized compound was characterized by AT-IR, $^1$HNMR, and MASS spectroscopic studies to confirm the structure of the synthesized derivatives.

The compounds synthesized were used for various pharmacological activities like acute toxicity, anti-inflammatory, anthelmintic, antimicrobial, antifungal and antioxidant activity.

The synthesized compounds along with their parent molecules were subjected for antimicrobial studies i.e., anti-bacterial study and anti-fungal study.

**Anti-bacterial activity**

Ampicillin sodium was used as standard for comparing the potency of the molecules. Compound N.n has showed more potent activity against all the gram positive and gram negative bacteria.
Compounds H.n, N.g, H.j, N.i and N.j were found to possess similar potency when compared to the standard compounds.

**Antifungal activity**

Naringin derivatives have shown mild to potent antifungal activity, which clearly suggest that replacement of a ketone moiety with a hydrazone or carbazone moiety increases the antifungal activity of the parent molecules. Compound N.n, N.j and N.g were found to be more potent when compared to the standard compound. Hesperidin derivatives have not shown promising antifungal activity when compared to naringin derivatives.

**In vitro antioxidant activity:**

*In-vitro* antioxidant studies were performed using ABTS, DPPH and nitric oxide assay. Ascorbic acid was used as standard in all the three methods.

Scavenging of ABTS radical cation activity showed that compounds H.c, H.i, H.k, H.m, N.a, N.h, N.k and N.l have shown moderate scavenging property with IC$_{50}$ value of 6.98, 6.95, 6.39, 6.89, 6.12, 6.43, 6.43 & 6.12µM respectively.

DPPH radical scavenging activity proves that compounds N.a and N.l has potent scavenging property with IC$_{50}$ value of 6.56 & 6.71µM respectively. Whereas compounds like H.h, H.i, H.j, H.k, H.l, H.m, H.n, N.i, N.k, N.l, N.n and N.r showed moderate scavenging property with IC$_{50}$ value of 7.94, 7.87, 7.45, 7.79, 7.88, 7.76, 7.99, 7.04, 7.45, 7.02 and 7.65µM, respectively.
Nitric oxide radical scavenging activity showed that compounds H.h, H.i, H.k, N.a, N.h, N.k, and N.l have potent scavenging property with an IC$_{50}$ value of 6.52, 5.96, 6.62, 5.32, 5.82, 6.21 and 6.47µM respectively.

**Anthelmintic activity**

Anthelmintic activity was performed using Indian adult earth worms (*Pheretima postuma*) at 0.1, 0.2, and 0.5 % concentrations and the time taken for paralysis and death was recorded. Compounds, H.g, H.h, H.o, H.p, N.b, N.h, N.g and N.q have shown very potent activity against the worms with the paralysis and death time very much low even when compared with the standard drug. Compounds H.a, H.c, H.i, H.k, H.l, H.n, H.q, H.r, N.c and N.e, have shown more or less equal potency with that of the standard drug.

**In-silico docking studies**

Protein - ligand interactions are studied by using GOLD 4.12 docking software. The docking results of the ligands with the protein 1CX2 (COX-II enzyme) showed both hydrophobic (vanderwaals interaction) and hydrogen bonding interaction. Ligand N.o, H.r, H.p, H.o, H.b, N.m, and N.p were found to have best gold fitness score of 56.70, 56.62, 56.36, 56.27, 54.02, 55.88 and 54.50 respectively.

**Anti-inflammatory activity**

The anti-inflammatory activity of compounds N.o, H.r, H.p, H.o, H.b, N.m, and N.p was carried out using male, Wister rats by carrageenan induced paw edema model using the standard drug diclofenac sodium (10mg/ml) and results showed that compound H.r
has most potent anti-inflammatory activity and the potency was comparable with the standard drug. Compounds H.b, H.o, N.p and N.o showed moderate anti-inflammatory activity. Compounds N.m, and H.p showed mild anti-inflammatory activity when compared with the standard drug.

The author concluded that compounds mentioned above were found to have good potency in the activity performed. Thus structures of these derivatives have to be optimized to explore the desired pharmacological activity.