

SUMMARY

The present work embodied in the dissertation is mainly concerned with the analysis of *Ajuga bracteosa* and *Rosa brunonii* isolation and characterization of isolated compounds, *in-vitro* activities including acetylcholine esterase inhibition, alpha- glucosidase inhibition, alpha-amylase inhibition, protease inhibition, antithrombotic, DNA damage protection and estimation of sun protection factor. *In-vivo* activities such as antidepressant, antidiabetic, antiulcer, and hepato-protective potential were carried out in *Wistar albino* rats to scientifically prove the folk-use of plants. Moreover, pre- treatment and co-administration effects of *Ajuga bracteosa* on pharmacokinetics of narrow therapeutic index antiepileptic drug i.e., carbamazepine, the effect of quercetin on pharmacokinetics of amiodarone and warfarin were studied in rats.

Both *Ajuga bracteosa* chloroform extract (ABCE) and *Rosa brunonii* fruit chloroform extract (RBFCE) showed acetylcholine esterase inhibition activity in a dose-dependent manner. The low IC₅₀ value ($499.326 \pm 21.30 \mu\text{g/mL}$) of RBFCE indicates its potential AChE inhibition activity compared to ABCE, ($747.80 \pm 10.70 \mu\text{g/mL}$). A dose-dependent inhibitory potential of ABCE and RBFCE was observed against α -amylase enzyme with an IC₅₀ value of $234.25 \pm 8.40 \mu\text{g/mL}$ and $322.64 \pm 17.40 \mu\text{g/mL}$, respectively. The ABCE revealed a significant inhibitory activity of α - glucosidase enzyme with an IC₅₀ value $100.14 \pm 2.30 \mu\text{g/mL}$ in comparison with an IC₅₀ value of RBFCE $248.93 \pm 1.62 \mu\text{g/mL}$. ABCE and RBFCE showed comparable protease inhibition activity with IC₅₀ = $465.42 \pm 10.20 \mu\text{g/mL}$ and $469.30 \pm 18.80 \mu\text{g/mL}$ respectively. ABCE demonstrated significant antithrombolytic potential with an IC₅₀ value = $751.76 \pm 186.20 \mu\text{g/mL}$ compared to RBFCE with an IC₅₀ value = $964.74 \pm 18.80 \mu\text{g/mL}$. RBFCE showed better DNA damage protection potential with increasing concentration compared to ABCE. The chloroform fraction of flowers (12.49) of *Rosa brunonii* showed the highest sun protection factor value followed by the ethyl acetate fraction of the stem (11.59).

Both medium (500 mg/kg) and high doses (750 mg/kg) of RBFCE showed promising antidepressant potential as indicated by the significant decrease in immobility time and increase in swimming time of mice compared to the control group. However, only a high dose (750 mg/kg) of ABCE significantly decreased the immobility time and increased the swimming time compared to the saline group indicating the better antidepressant potential of RBFCE compared to ABCE. Results of antidiabetic activity indicated that

alterations in glucose level of 500 mg/kg, 750 mg/kg and 1000 mg/kg of ABCE treated rats were found to be -25.18% ($p < 0.05$), -32.53% ($p < 0.01$) and -45.02% ($p < 0.01$) respectively. Similarly, reduction in glucose level of 500 mg/kg RBFCE, 750 mg/kg and 1000 mg/kg treated rats were found to be -19% ($p > 0.05$), -21.43% ($p > 0.05$) and -27.21% ($p < 0.05$) respectively indicating the better antidiabetic potential of ABCE than RBFCE.

Results of antitussive activity demonstrated that ABCE prominently reduced the number of coughs in a dose-dependent manner compared to RBFCE. Antiulcer activity results demonstrated that ABCE significantly reduced the ulcer index and increased protection rate compared to RBFCE treated animals. Both extract treatments increased gastric pH, gastric mucus content, and total protein while gastric juice volume and total acidity were decreased in dose-dependent manner with higher magnitude in ABCE treated animals. Oral administration of ABCE showed a significant gastro-protective effect than RBFCE due to its anti-secretory and cytoprotective mechanism. Moreover, both RBFCE and ABCE displayed significantly reduced Rifampicin/Isoniazid induced toxicity at high doses in liver and kidney tissues as indicated by the normalized serum biochemical markers and histopathological investigations.

Rosa brunonii fruit and *Ajuga bracteosa* contained Fe (7 mg), (11 mg), and Ca (108 mg, 146 mg) respectively. Cr was detected at a concentration of 34 mg and 13 mg in *Ajuga bracteosa* and *Rosa brunonii* fruit respectively. Mn, Mg and K were found to be 7 mg, 114 mg and 213 mg in *Ajuga bracteosa*. All concentrations were determined per 100 gm of plant material. Phytochemical analysis of various fractions of *Ajuga bracteosa* and *Rosa brunonii* fruit indicated the presence of flavonoids and phenolic compounds in polar fractions. The physicochemical parameters including loss on drying and ash value for *Ajuga bracteosa* were found 11.54% and 7.98% whereas for *Rosa brunonii* fruit 12.09% and 6.44% respectively. Similarly, water-soluble ash values for *Ajuga bracteosa* and *Rosa brunonii* fruit are 1.04% and 1.46% respectively. However, acid insoluble ash for *Ajuga bracteosa* and *Rosa brunonii* fruit were 0.79% and 4.96% respectively. Quantitative liquid chromatographic analysis of ABCE indicated stigmasterol (2.9 mg/g), sitosterol (2.1 mg/g), and ursolic acid (1.3 mg/g). Quercetin and kaempferol were

found 3.2 mg/g and 2.70 mg/g of extract in ABCE respectively. However, quercetin was found 2.45 mg/g of extract in RBFCE. Phytochemical studies of *Rosa brunonii* fruit resulted in the isolation of two new source compounds, which had never been isolated so far from this investigated source. The compounds isolated for the first time from *Rosa brunonii* fruit were 2,3-trans-catechin (1) and quercetin-3-O-glucoside (2). The structure of these compounds was determined by Mass, IR, ^1H , and ^{13}C NMR spectroscopy and by comparison with the published data of the closely related compounds.

Non-compartmental pharmacokinetic analysis showed an increase in C_{max} , $\text{AUC}_{0-\infty}$, MRT, and $t_{1/2}$ with a decrease in t_{max} , V_d and Cl of carbamazepine in both pre-treated and co-administered groups vs controls. An increase in carbamazepine concentration in the liver tissue of both pre-treated as well as co-administered animals was observed compared to the control. Similarly, in the pre-treated group, amiodarone C_{max} and $\text{AUC}_{0-\infty}$ were increased while t_{max} , $t_{1/2}$, and Cl declined compared to the control. In co-administered group, compared to controls, C_{max} and $\text{AUC}_{0-\infty}$ were raised, while t_{max} , $t_{1/2}$, and Cl were reduced. Furthermore, drug concentration was increased in the lung tissue of both treated groups, relative to the respective controls. Likewise, in the pre-treated group, C_{max} , $\text{AUC}_{0-\infty}$, t_{max} and $t_{1/2}$ were increased, while V_d and Cl of warfarin were decreased in comparison with the control. Similarly, in co-administered animals, C_{max} , $\text{AUC}_{0-\infty}$, t_{max} and $t_{1/2}$ were increased, while a decline in V_d and Cl was noticed for warfarin.