ABSTRACT

The present Ph.D dissertation deals with the isolation and structure elucidation of potential anti-tumor agents from some members of family Asteraceae and Lauraceae. *Bidens biternata*, *Saussurea atkinsonii*, *Senecio chrysanthemoides* and *Senecio ledebourii* of family Asteraceae, while *Cinnamomum tamala* and *Cinnamomum zeylanicum* of family Lauraceae were selected for the studies. This is the first report of *in vitro* anti-tumor activity of these plants against human ovarian cancer cell line (A-2780) assessed by alamar blue dye assay. Most of them exhibited moderate to excellent anti-tumor activities which were also associated with their cytotoxicity against normal fibroblast baby hamster kidney cells (BHK-21).

The selected plants were subjected to bioassay guided fractionation which resulted in the isolation of three flavonoids namely 5,7-dihydroxy-2-(4'-hydroxy phenyl)-4H-1-benzopyran-4-one (1), 2-(3',4'-dihydroxyphenyl)-3,5,7-trihydroxy-4H-chromen-4-one (2) and 3,5,7-trihydroxy-2-(3',4',5'-trihydroxyphenyl)-4-chromenone (3) from *B. biternata*. These flavonoids exhibited significant anti-tumor activity in the order of $2 < 3 < 1$. The bioassay directed isolation of *S. atkinsonii* yielded four compounds; 3,5,7-trihydroxy-2-(4'-hydroxyphenyl)-4-chromenone (4), 3-ammonio-4-hydroxy benzoate monohydrate (5), 6,7-dihydroxy-2-chromenone (6) and decahydro-3,6,9-tris (methylene) azuleno [4,5] furan-2-(3H)-one (7). Compounds 5 and 6 showed strong anti-tumor activity with IC$_{50}$ values of $1.38 \times 10^3$ and $2.55 \times 10^3$ mg/mL respectively. Compound 8 [(E)-3-(4-hydroxy-3-methoxy phenyl)-prop-2'-enoic acid] and 9 [4-hydroxy-3,5-dimethoxy benzoic acid], isolated from *S. chrysanthemoides*, were inactive against human ovarian cancer cell line, while compound 10 exhibited significant activity with IC$_{50} = 7.59 \times 10^3$ mg/mL. Bioassay-guided fractionation of *S. ledebourii* yielded compound 11 [(E)-3,4',5-trihydroxy-trans-stilben], 12 [7-hydroxy-2H-1-benzopyran-2-one] and 13 [7-hydroxy-6-methoxychromen-2-one], among which compound 11 exhibited significant inhibitory activity with IC$_{50} = 2.14 \times 10^3$ mg/mL. The compounds isolated from *Senecio* species showed anti-tumor activity in the order of $8 < 9 < 13 < 12 < 10 < 11$. Four compounds were isolated from *C. tamala* extracts which were identified as caryophylene oxide (15), 1,7,7-trimethylbicyclo [2.2.1] hept-2-yl acetate (16), 3-(4-hydroxy phenyl)-2-propenoic acid (17) and 4-hydroxy-3-methoxy benzoic acid (18), while 6-methoxy-4-methyl coumarin (33), 7,8-dihydroxy-4-methyl
coumarin (34) and ethyl 3,4-dihydroxy benzoate (35) were purified from the extracts of C. zeylanicum. Compound 36 [5-isopropyl-2-methylphenol] was isolated from the essential oil of C. zeylanicum bark. The activity of these eight isolates of Cinnamomum species was observed in the order of 18 < 17 < 34 < 33 < 15 < 36 < 35 < 16.

GCMS analysis of column chromatography fractions (CT₁, CT₂ and CT₄) of C. tamala methanol extract resulted in the identification of eight compounds along with fifteen major components from other seven sub fractions (CT₃-A to CT₃-G ) of a CC fraction CT₃. Column chromatography of CZ₂ of C. zeylanicum chloroform extract yielded three sub fractions (CZ₂-A to CZ₂-C). A few major components of these sub fractions were also characterized with the help of GCMS technique and anti-tumor bioassays.

The isolates obtained in this research work can be classified as four flavonoides (1, 2, 3 and 10), five coumarins (6, 12, 13, 33 and 34), seven phenolic compounds (4, 8, 9, 11, 17, 18 and 35) and one sesquiterpene lactone (7). Anti-tumor potential of the four flavonoids was observed in the order of activity (2 < 10 < 3 < 1). The coumarins showed moderate cell growth prevention potential against A-2780 cells with order of activity 6 > 34 > 12 > 33 > 13. Sesquiterpene lactone was most active one and only two phenolic compounds i.e. 11 and 35 proved as good anti-tumor agents and exhibited significant inhibitory activity against human ovarian cancer cells with comparatively less cytotoxicity against BHK cells.