ABSTRACT

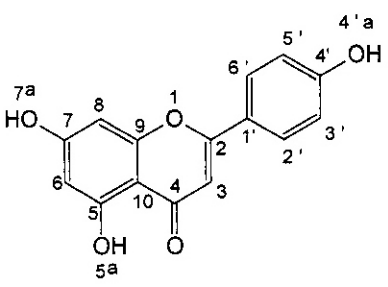
The present Ph.D dissertation deals with the isolation and structure elucidation of potential anti-tumor agents from some members of family Asteraceae and Lauraceae. *Bidens biternata*, *Saussurea atkinsonii*, *Senecio chrysanthemoides* and *Senecio ledebourii* of family Asteraceae, while *Cinnamomum 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 1.38×10^{-3} and 2.55×10^{-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 (CT_1, CT_2 and CT_4) of *C. tamala* methanol extract resulted in the identification of eight compounds along with fifteen major components from other seven sub fractions (CT_3–A to CT_3–G) of a CC fraction CT_3. Column chromatography of CZ_2 of *C. zeylanicum* chloroform extract yielded three sub fractions (CZ_2–A to CZ_2–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**. Sesqueterpene 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.



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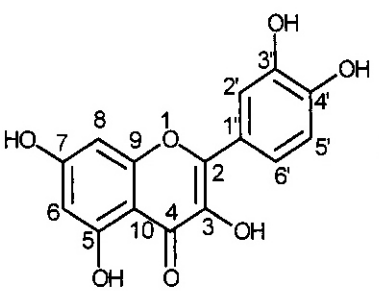

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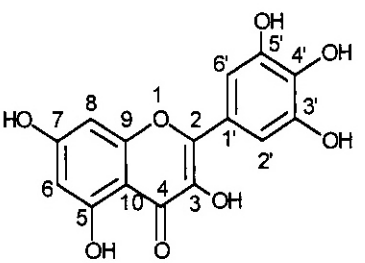

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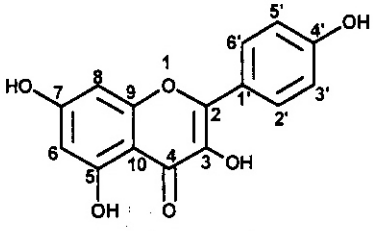

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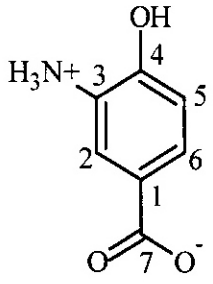

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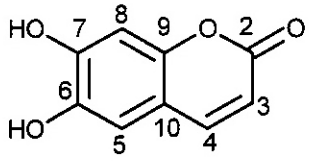

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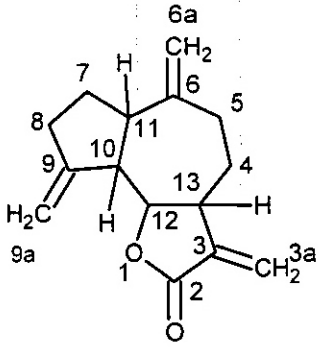

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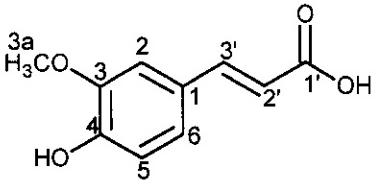

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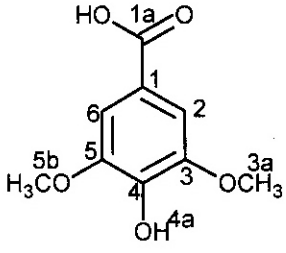

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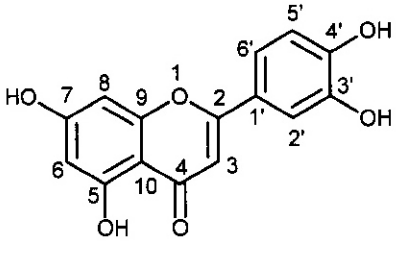

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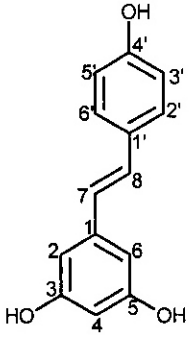

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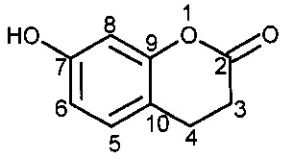

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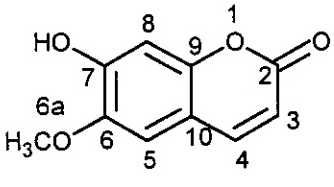

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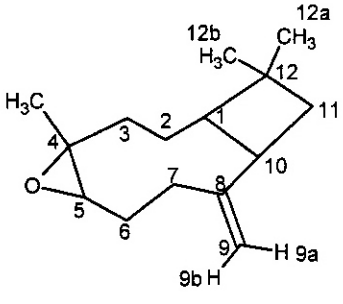

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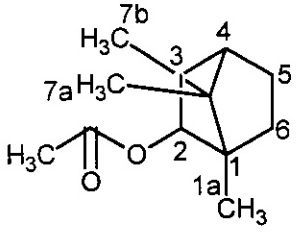

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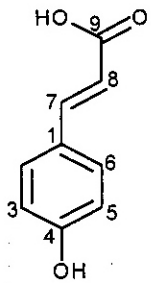

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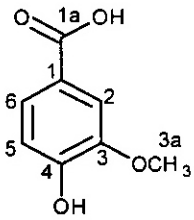

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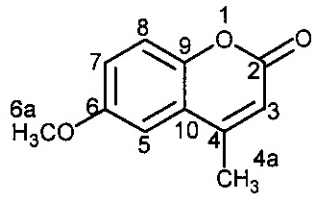

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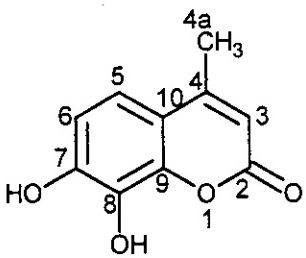

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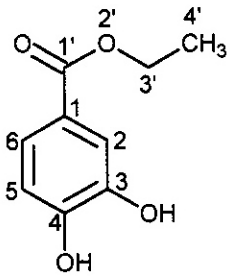

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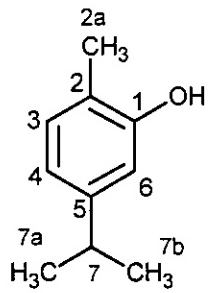

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