

STAGES OF GROWTH OF CELLS IN TUMOR

Flavonoids are most widely found in photosynthesizing plant cells. These are the indispensable part in human and animal diet and cannot be synthesized within body. In recent years, there has been an upswing concern in the therapeutic potential of flavonoids. These are mainly due to the presence of phenolic groups [17,18]. Various edible plants have been linked to the treatment of cancer [19]. Various plant-derived agents such as paclitaxel, docetaxel; vinblastine, vincristine; and toptotecan, irinotecan, and etoposide are currently being used for the treatment of cancer [20-22].

Plants have various flavonoids which are biologically very active and possess various therapeutic properties, which outline its necessity for determination [23]. Flavonols such as catechin, epicatechin, and epigallocatechin from tea have been extracted [24]. Certain flavones such as chrysin, apigenin, rutin, luteolin, and luteolin glucosides are found in the fruit skins, red wine, buckwheat, red pepper, and tomato skin [25-28]. Flavanols such as kaempferol, quercetin, myricetin, and tamarixetin are found in onion, red wine, olive oil, berries,

and grapefruit [29]. Citrus fruits, grapefruits, lemons, and oranges possess flavonones such as naringin, naringenin, taxifolin, and hesperidin [30,31]. Soybean consists of isoflavone such as genistein and daidzein [32].

Polyphenols found in tea especially in green tea have shown to reduce the risk of cancer [33]. Curcumin in turmeric has been found to affect various multicellular signaling pathways, which are involved in proliferation, invasion, survival, apoptosis, and inflammation [34]. Various other plants and their phytochemicals effective against cancer are listed in Table 2.

Table 1: Classification of flavonoids

| S. No. | Groups | Subgroups |
|--------|---------------|---|
| 1. | Flavonoids | Flavan Flavanone Flavone Flavonol Dihydroflavonol Flavan-3-ol Flavan-4-ol Flavan-3,4-diol |
| 2. | Isoflavonoids | Isoflavan Isoflavone Isoflavanone Isoflav-3-ene Isoflavanol Rotenoid Coumestan 3-aryl-coumarin Coumaronochremene Coumaronochromone Pterocarpan |
| 3. | Neoflavonoids | 4-aryl-coumarin 3,4-dihydro-4-aryl-coumarin Neoflavene |

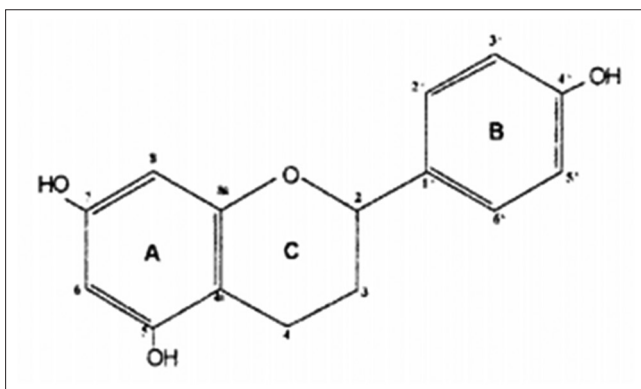


Fig. 1:

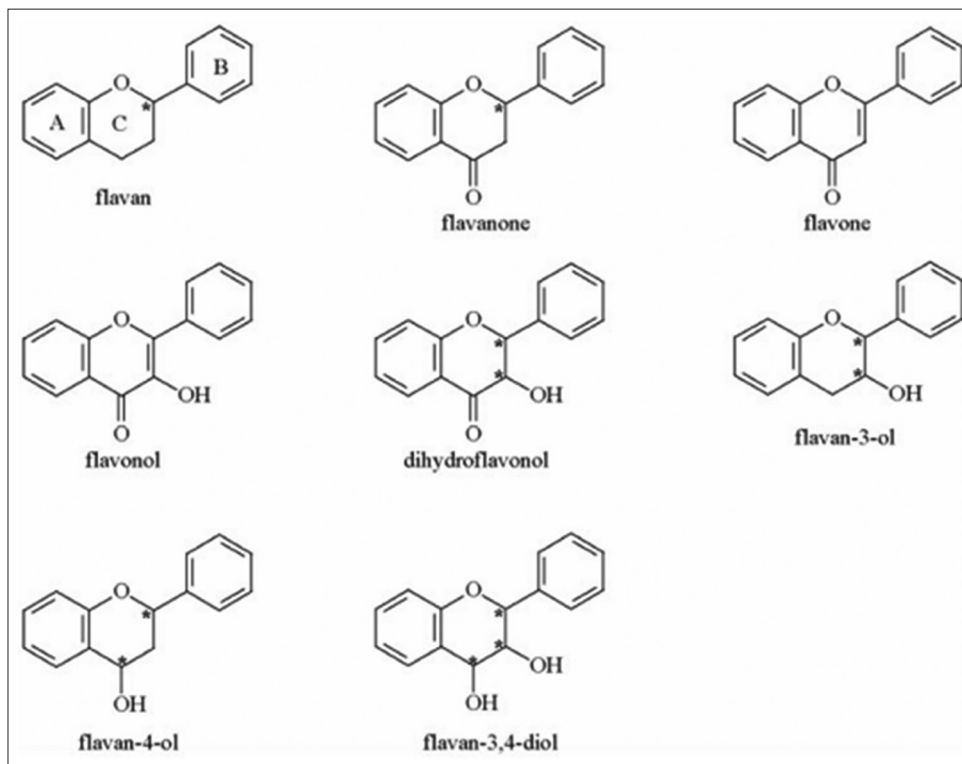


Fig. 2:

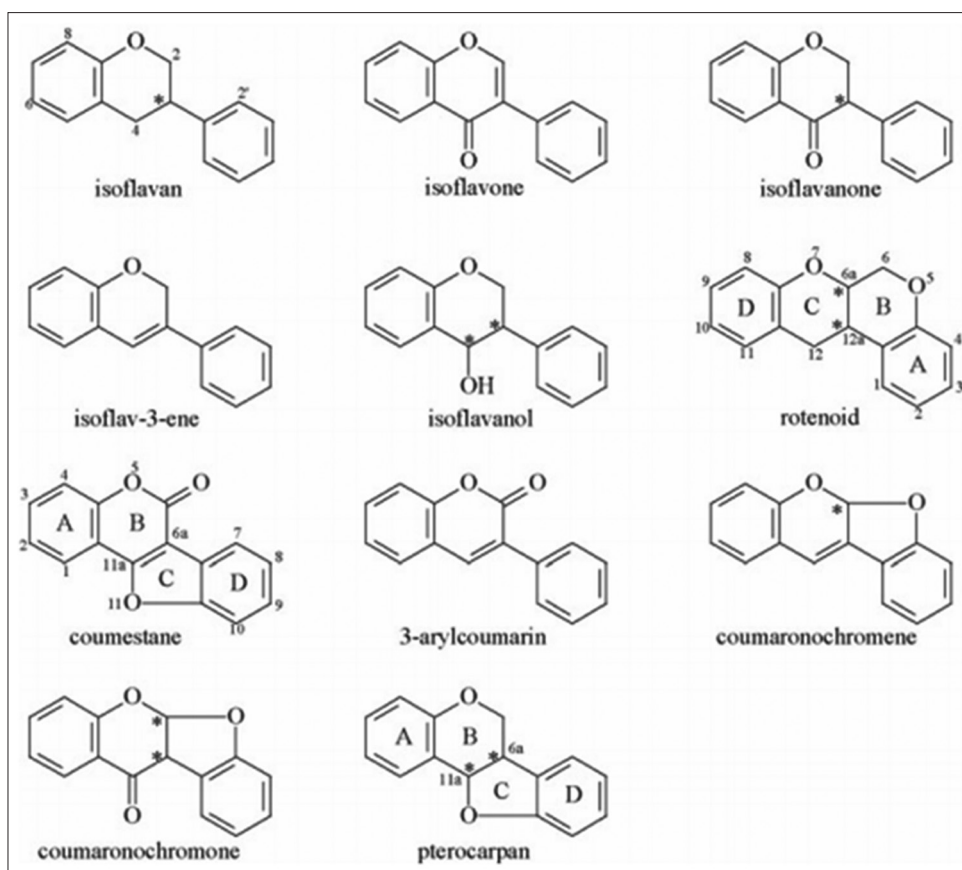


Fig. 3:

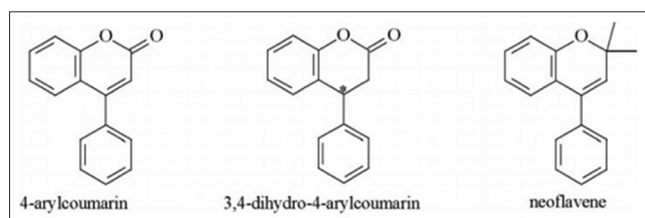


Fig. 4:

VARIOUS FLAVONOIDS IN FOOD

In vitro studies

Many researchers have conducted various *in vitro* studies on the potential anticancer activity of flavonoids. Biphasic effects of isoflavones have been seen in proliferation of breast cancer cell culture. At concentration above 5 mM, genistein showed concentration-dependent ability to inhibit growth and estrogen stimulated breast cancer cell proliferation. 28 flavonoids were studied by Hirano *et al.* against acute myeloid cell line HL 60 and were compared with antiproliferative activity and cytotoxicity with four clinical anticancer agents. Out of these 28 flavonoids, eight shows suppressive effects on HL 60 cell growth. The rest had potent anticancer activity [42]. 55 flavones were evaluated by Cushman and Nagarathnam and studied their toxicity in five cancer cell cultures and were found effective against A-549 lung carcinoma, MCF-7 breast carcinoma, HT-29 colon adenocarcinoma, SKMEL-5 melanoma, and MLM melanoma [43]. 27 out of these were of citrus origin and were found to inhibit tumor cell proliferation.

In vivo studies

Flavonoids have also shown to exhibit anticancerous activities *in vivo* studies. They may inhibit carcinogenesis in any stage of

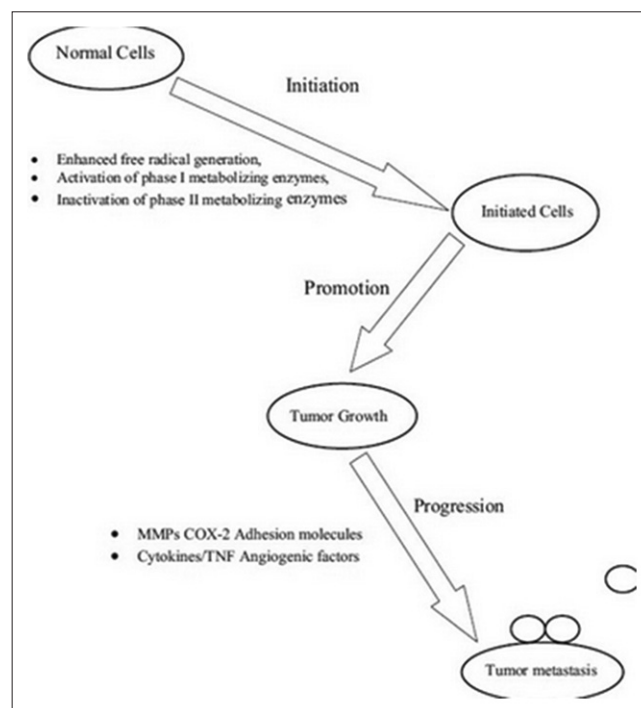


Fig. 5:

carcinoma. Animal and other cellular model investigations showed that certain flavonoids inhibit tumor initiation and progression. A novel research showed that fermented soy milk which contains large amounts of genistein and daidzein which were given to rats

Table 2:

| S. No. | Source | Phytochemicals | References |
|--------|---|-------------------------------------|------------|
| 1. | Broccoli, sprouts, cabbage, kale | Sulforaphane | [35] |
| 2. | Broccoli, cabbage, cauliflower, mustard, and radish | Indole-3 carbinol, diindolylmethane | [36] |
| 3. | Soy compounds | Genistein, Soy isoflavones | [37] |
| 4. | Wasabi, horseradish, mustard, radish, Brussels sprouts, watercress, nasturtiums, capers | Isothiocyanate | [38] |
| 5. | Red wine, peanuts, and certain berries | Resveratrol | [39] |
| 6. | Garlic, chives, and leeks | Organosulfur compounds | [40] |
| 7. | Tomato products | Lycopene | [41] |
| 8. | Citrus fruits and buckwheat | Quercetin | |

of 7 weeks of age showed to inhibit mammary tumorigenesis which was induced artificially by 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine [44].

Mammographic breast density can be used as biomarkers for estrogenic and anti-estrogenic effects of a particular treatment in breast tissue. Consuming dietary supplements including red clover-derived isoflavonones for 12 months did not show any increase in mammographic breast density in women experiencing menopause suggesting that there are no effects of estrogenic and anti-estrogenic effects on the breast [45].

CONCLUSION

Flavonoids have a wide range of therapeutic effects. The impact of flavonoids has been seen widely during the avalanche of immunological events which are correlated with the advancement and progression of cancer. They have regulatory role on various hormones [46]. A methodical mechanism is to be developed so as to understand mechanism of action of flavonoids, when they enter various cell organelles and tissues. Flavonoids are probable to deflect various biological events in cancer including apoptosis, vascularization, cell differentiation, and cell proliferation. Various dietary flavonoids show antitumor activity during *in vivo* studies whereas these show repression *in vivo* studies.

Various potent flavonoids are to be studied and extracted for elucidating various other natural ways in treating cancer. They are gaining interest due to their wide variants and number of members. These are reported to be effective in pathogenesis of majority of diseases [47]. Further studies should be conducted so as to validate the traditional ways of treating cancer. In the past, many efforts are made to get various anticancerous plants containing flavonoids and further studies are to be made to get satisfactory results. For these, a number of medicinal plants can be screened and can be further worked on so that *in vitro* and *in vivo* studies can be conducted providing new insights for fighting against cancer.

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