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FRUITS AND VEGETABLES – CHEMOPREVENTION, ANTIDIABETIC, PROPERTIES

Nutritional Science

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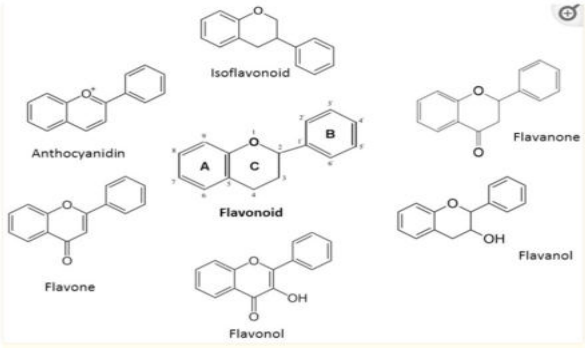
KEYWORDS

Flavinoids Chemoprevention Fruits And Vegetables

Flavonoids are rich in plant products are polyphenols [9 17 18 21 29 46 47 52 62 69]. They are present in different varieties of food but abundantly available in food like fruits vegetables tea and spices. More than 8000 varieties of polysulphides exist, in this the major varieties mainly are Flavonoids, polyphenolic amides, phenolic acids and others.[1-78]

Examples of polysulphides rich in

- Flavonoids are rich in quercetin and catechins -Fruits[1,38,9,20,22,29,35,36,40, 41,51,54,58,64,67,76], black and green tea[4,5,6,9,16], wine, among vegetables highest level present in beans, olives, onions shallot, spinach cocoa based shallot, onions plums apple, cherries, berries. [[1,3 8,9,20,22,29,35,36,40,41,51,54,58,64,67,76]
- Polyphenolic amides – Capsaicinoids -chili, peppers.[9,17,18,21,29,, 46,47,52,62,69]
- Phenolic acids – lignan's and stilbenes in vegetables and whole grains.
- Other -resveratrol in red wine and ellagic acid – berries Flavonoids[1,3,8,9,20,22,29,35,36,40,41,51,54,58,64,67,76] are phenolic compounds[9,17,18,21,29,46,47,52,62,69], secondary metabolites'[1] ,sub divided into 6 types -Isoflavonoids[9] ,flavanols[14,18,19,29,31] and anthocyanidins[9,29,68,71] present in green biota. Fig 1



Functions

1. Wide variety of anticancer effects - reactive oxygen species - induce apoptosis,autophagy,inhibit the action of cancer cell proliferation and cell cycle ,invasiveness[2,3,9,11,13,27,28,29,38,48,66,74,75,76]
2. Dual action – Homeostasis -potent pro-oxidants in cancer cells activates the apoptotic pathways and downward pro inflammatory signaling pathway.[2,3,9,11,13,27,28,29,58]

Chemical properties : Potent antioxidant ,anti -inflammatory, immunomodulator ,anti-tumour genic activity.[2,3,911,13,27,28,29,38]

Chemical structures : Flavonoids formed by the basic flavan skeleton – 15 carbon phenylpropanoid (C6-C3-C6 system) two aromatic ring linked by a heterocyclin pyran ring,degree of oxidation and linking chain unsaturation flavonoids[1,38,9,20,22,29,35,36,40,41 ,51,54,58,64, 67,76], flavanones[9], flavanols[14,18,19,29,31], flavones and anthocyanidins.(Fig 1)[9,29,68,71]

Genistein[10,9,29,49,56,59] and daidzein[9,29,34,44] are two major Isoflavonoids[(Fig 2)

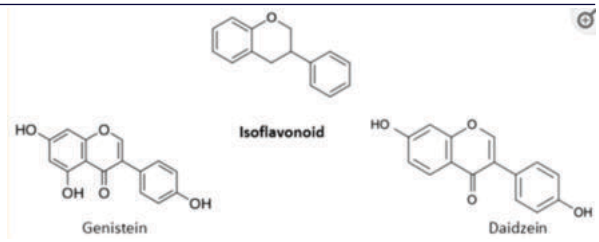
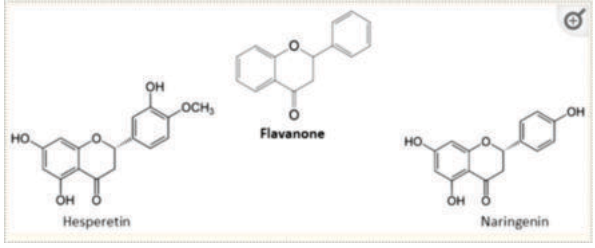


Fig:2

Hesperetin[9,29,43,74,77,78] and naringenin[32,45] are two main flavonones (Fig 3)



Flavanols Contains Quercetin[7,9,29,50,55,66,72] and kaempferol, myricetin isorhamnetin ,fistein and galangin in lesser amounts .[9,15,23,29,73]

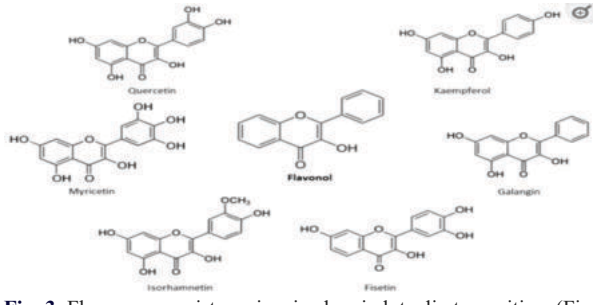


Fig 3 Flavones consists apigenin,chrysin,luteolin,tangeritin .(Fig 4)[9,29,33,46,57,61,70]

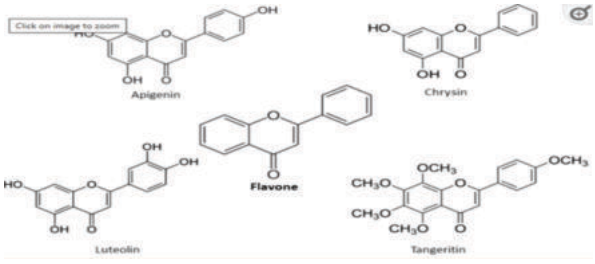


Fig4 Anthocyanin contains cyanidin, delphinidin, malvidin, pelargonidin,petunidinpeonidin.(Fig 5)[9,11,12,26,29,36,60,66,68,71]

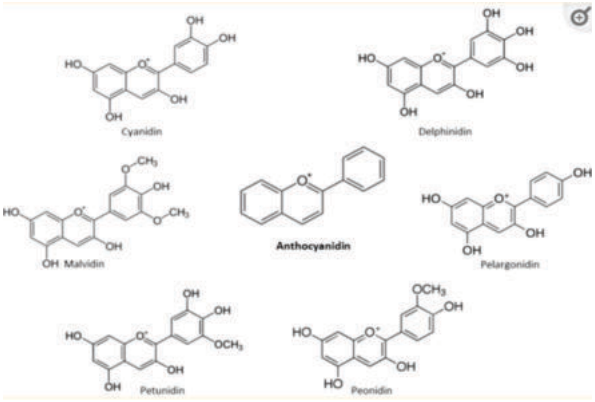
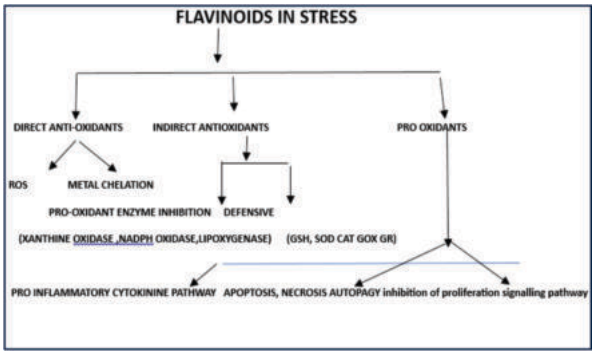


Fig 5 Flavonoids are weak hydrophobic, lipophilic and cross the barrier reaches cellular and mitochondrial membrane and act as protonophores[1-78]

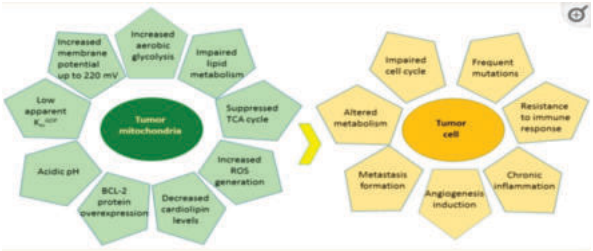
Action of Flavonoids is explained in Fig 6 [1-78]



ANTI TUMOR ACTIVITY:
1.FREE RADICALS – ABILITY
2.CELLULAR METABOLISM
3.OXIDATIVE STRESS - Anti oxidant always work against oxidative stress induced syndrome
4.MOLECULAR METABOLISM activity is not known, further action is required

Heterogenous diseases are characterized by uncontrolled proliferation and impairment of cell cycle leading to growth of abnormal cells that undergone antioxidant, hypoxia, mutation and lack apoptotic function, chronic inflammation ,induction of angiogenesis main internal causes, external causes includes stress, pollution smoking, radiation rays exposure and internal metastasizes to other organs of the body ,this are the feature is seen in cancer.(Fig 7).[1-37]

Metabolic diseases include cancer there is emergence of evidence in this aspect.[20-37] However, this aspect had driven a new trend in research, evolved in introspecting the mechanism of action of flavoids to anti tumorgenic action .cellular activities were depicted (Fig 7)[1-78]



Diabetes mellitus(DM) is also treated with antioxidants. In the study by Dienaite et al proposed that Salvia Africana-lutea showed that polyphenolic extracts from root and leaves of Paeonia officinalis had antioxidant and free radical scavenging activity, they had performed analysis to found the mechanism of action and identified on DM. *α-AMYLASE* inhibition is identified so used as antidiabetic agent[1-78].The analysis performed by UPLC-Q/TOF results in the HPLC - DPPH compound that is anti oxidant present in Rubus idaeus L (raspberry) extract obtained showed rich in polyphenols by HR-HPLC -ESI -Qtof-ms/ms analysis and It had antioxidant and anti-diabetic properties .Valvcheski et al proposed that the antidiabetic activity due to action against diabetes induced oxidative stress identified in olive oil due rich hydroxytryosol levels.[1,3,8,9,20,22,29,35,36,40,41,51,54,58.60]

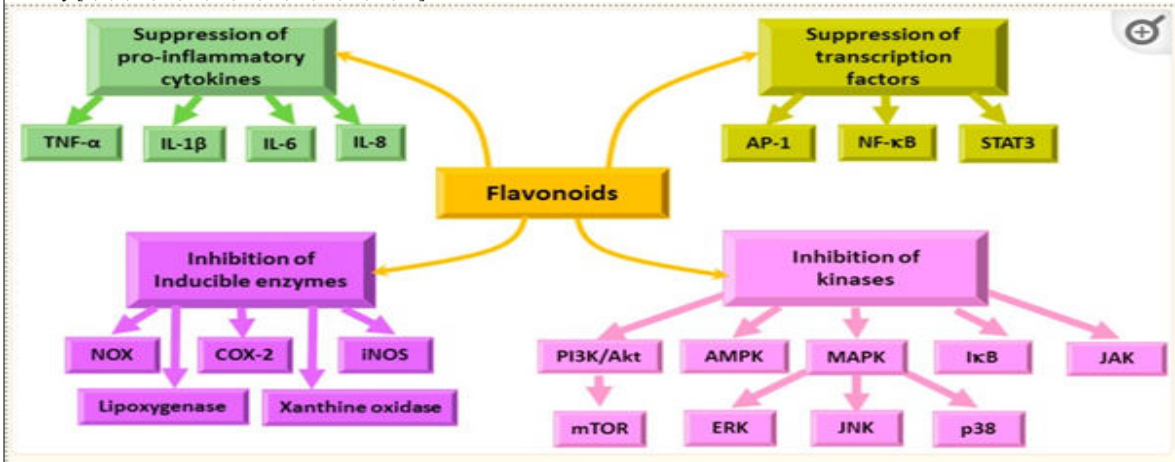
Bioavailability of Flavonoids

Nutrients interactions are possible with flavonoids and helps in hydrolysing enzymes mainly amylase and glucosidases act transporter also. Improves the gut motility by secretion of bile salts augmentation, mainly fat diet improves and proteins rich diet reduces flavonoids bioavailability. Gut intestinal or colon microflora helps consumption of flavonoids. Metabolism occurs in small intestine liver and kidney. Activites are explained in Table 1.Half life is 1 to 2hrs is high in plasma, less half life for flavonols. [1-7,9,20,22,29,35,36,40,41,52,54,58,64,67,76]

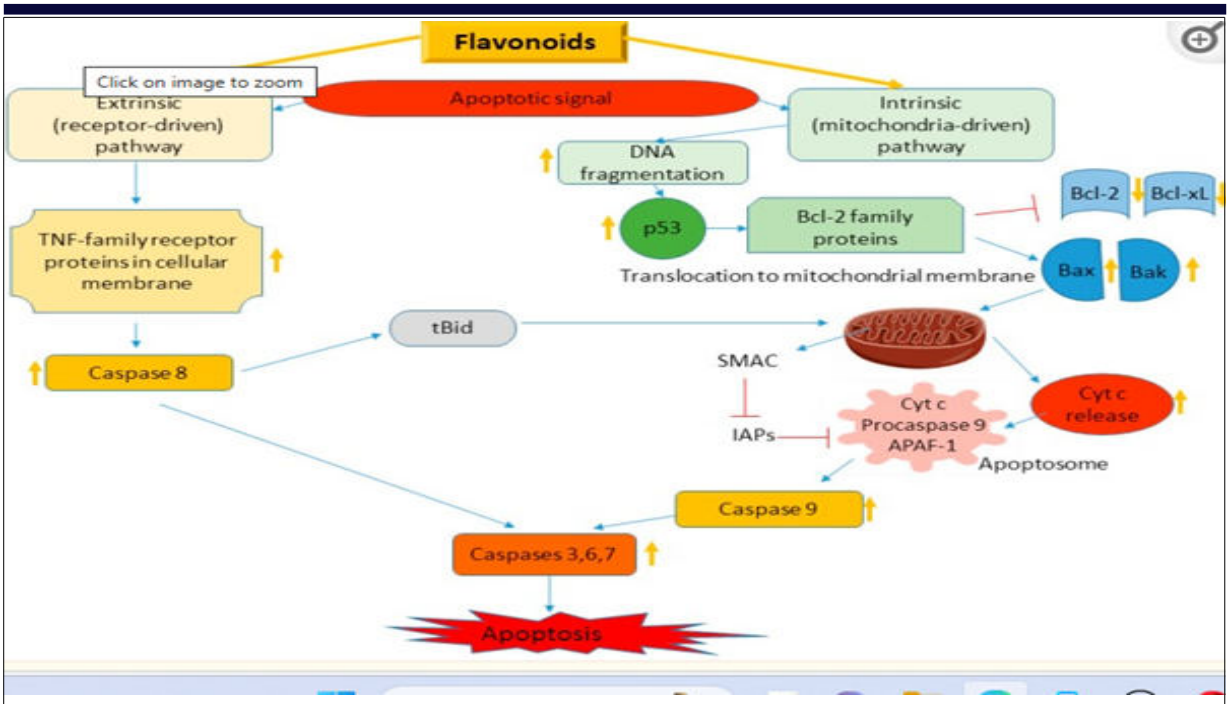
BIOLOGICAL ACTIVITIES OF FLAVINOIDS
METHYLATION
SULFATION
GLUCRONIDATION

Table -1 Flavinoids, Mechanism Of Action Molecular Markers

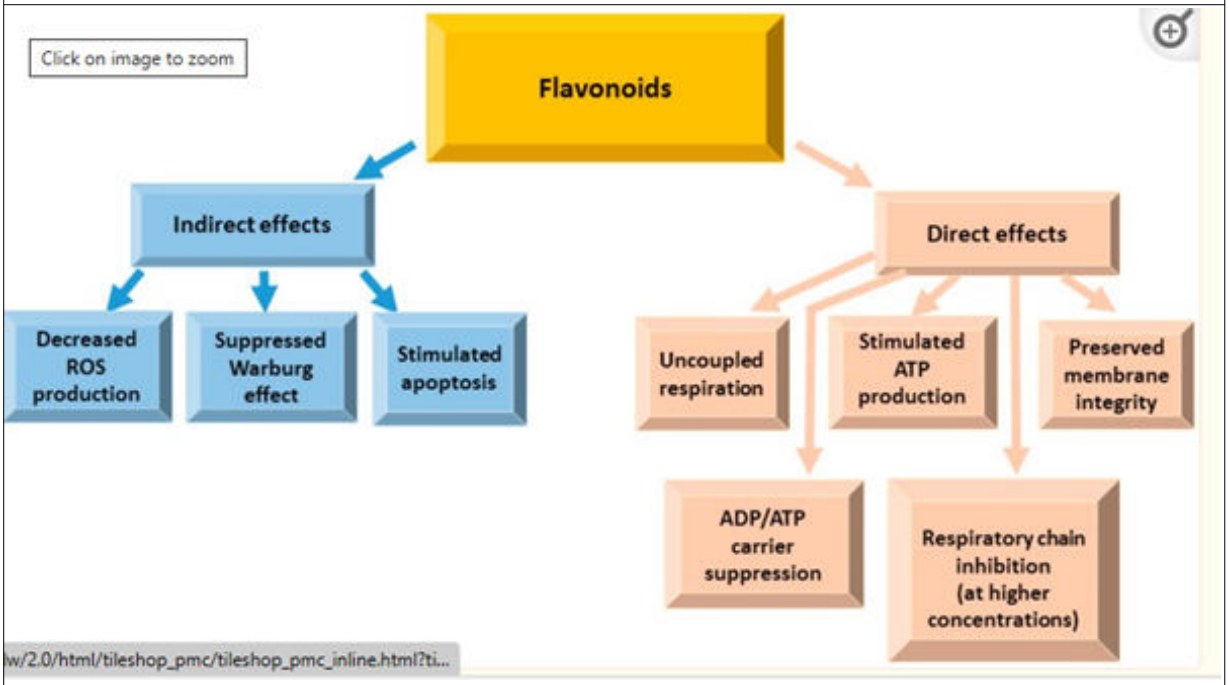
Because flavonoids modulate the microbiota, they suppress inflammatory markers in the gastrointestinal tract by downregulating the transcription factor NF-κB signaling pathway. This represents a potentially effective therapeutic approach to prevent chronic diseases and control inflammation.[1-7,9,20,22,29,35,36,40,41,52,54,58,64,67,76]Since chronic inflammation frequently occurs before tumor growth, flavonoids' anti-inflammatory properties may be crucial for reducing inflammation and boosting immune cell antitumor activity.[2,3,9,11,13,27,28,29,38,48,66,74,75,76]



ISOFLAVONE – GENISTEIN [9,10,29,49,56]	INIHIBITS CELL PROLIFERATION-G2/M-BREAST CARCINOMA(CA)	ROS DEPENDENT APOPTOSIS [2,3,9,11,13,27,28,29,38,48,66,74,75,76]
	MCF-7 BREAST	ROS GENERATION



By upregulating and downregulating anti-apoptotic proteins, Daidzein caused apoptosis in the HCCSK-HEP-1 cell line. This led to the release of cytochrome c from mitochondria and the activation of a subsequent apoptotic cascade involving caspases 3 and 9.[9,29,34,44]



Alzheimer's disease is another chronic illness linked to oxidative stress in addition to cardiovascular diseases . The protective effect of epicatechin against oxidative stress-induced neuronal damage was evaluated in vivo by Diaz et al. Specifically, they showed that the administration of epicatechin to rats administered with Aβ25–35 injections decreased inflammation, oxidative stress, and neurotoxicity in the hippocampal regions.
Additionally, the treatment of epicatechin reduced the immunoreactivity to heat shock protein (HSP)-60, -70, and -90 as well as neuronal death in the hippocampal region known as Cornu Ammonis 1 (CA1), supporting an improvement in spatial memory performance. [4,5,6,9,16,24,25,29,53]

α-amylase was inhibited by epigallocatechin galate produced from oolong tea . Reduced activity of α-glucosidase, pancreatic lipoprotein lipase, and amylase in the lumen of the gastrointestinal tract would result in a reduced absorption of glucose from complex carbohydrates and fatty acids from triglycerides.-antidiabetic .[4,5,6,16,24,25,29,53,74,75,76]

Interleukin-17A (IL-17A), a pro-inflammatory cytokine, has been demonstrated to be inhibited by cyanidin . In vitro, pelargonidin inhibited the activation of ERK½ or NF-κB and the synthesis of TNF-α or IL-6 . In HT-29 colorectal adenocarcinoma cells, the anthocyanins from cocoplums suppressed the generation of TNF-α and IL-6 as well as the activation of NF-κB or ERK ½ .
The activation of NF-κB via MAPK signaling pathways in MCF-7 human breast cancer cells was inhibited by delphinidin. [2,3,9,11,13,26, 27,28,29,36,38]

FLAVANONE -HESPERETIN [9,29,43,74,77,78]	INDUCES APOPTOSIS 1.GALL BLADDER CARCINOMA 2.ESOPHEGEAL CARCINOMA 3.HEPATOCELLULAR CARCINOMA 4.MCF-7	ACTIVATING MITOCHONDRIAL APOPTOTIC PATHWAY -ROS PRODUCTION
FLAVANONE-NARINGENIN	CHORIOCARCINOMA JAR AND JEG 3 CELL LINES HUMAN EPIDERMOID CARCINOMA(CA) IN PROSTATE CA PC3AND LNCaP CELL LINE	GENERATION OF ROS AND ACTIVATION OF SIGNALLING INDUCES APOPTOSIS ACTS AS SUPEROXIDE DISMUTASE CATALASE,GLUTATHIONE IN CHRONIC CA
COCOA CATECHINS AND PROCYANIDINS[5 67 11 13 16]	OVARIAN CANCER -EPITHELIAL IN ORIGIN	INHIBITION DNA PROLIFERATION APOPTOSIS ACTIVATES THE ERK1 /2 PATHWAYS PROOXIDANT PROPERTIES-INCREASES GLUTATHIONE PERIOXIDASES AND HEPG2 CELL REDUCES ROS PRODUCTION
FLAVANOL QUERCETIN – CHEMOPREVENTION – IN THE STUDIES OF JEON J.S ET AL2019, RATHER ET AL 2019 TANG ET AL 2019 PROPOSED THAT SUSBSTANCE QUERCETIN INHIBITS THE PROLIFERATION OF HEPATOCELLULAR CARCINOMA HEP G2 CELLS DECREASING THE INTRACELLULAR ROS . GASTRIC CANCER ,HUMAN BREAST CANCER MCF -7 -SUBSTANCE QUERCETIN HAS EFFECT . QUERCETIN AND NARINGENIN PREVENTED THE LOWERED MRNA EXPRESSION OF LIVER IL-4, P53 AND BCL-2 IN A DIETHYLNITROSAMINE/2-ACETYLAMINOFLUORENE-INDUCED HEPATOCARCINOGENESIS MODEL IN RATS. NARINGENIN INHIBITED THE MIGRATION OF BREAST CANCER MDA-MR-231 CELL LINE VIA MODULATION OF INFLAMMATORY AND APOPTOTIC SIGNALING PATHWAYS[1-78]		
FLAVONOL KAEMPFEROL-COLORECTAL CANCERS – HCT116 HCT-15 AND SW480 [9,14,15,18,19,23,29,31,75] DISADVANTAGE – CYTOTOXIC EFFECTS,	ARREST S PHASE TNF-alpha induced IL-8 promoter activation and gene expression in HEK 293 cells Suppresses the MAPK and NF-κB signaling pathways	ROS LEVEL MODULATION INDUCED APOPTOSIS
FLAVONES – APIGENIN AND LUTEOLIN [57,61] CHRYSIN - CHORIOCARCINOMA -ES2 AND OV90 [9,29,33,46,70]	OVARIAN CANCER CELL LINES -A2870 OVCAR-3, CERVICAL CANCER HUMAN PAPILLOMA VIRUS {HPV +VE}18 &16 -SIHa CaSKi {HPV -VE} 18 &16	APOPTOSIS
ANTHOCYANIN – ANTIOXIDANT CAPACITY IN SERUM CYANIDIN – CELL DEATH INDUCER – ROS MODULATION DU145 AND LNCAP -PROSTATE CANCER AND COLORECTAL CANCER CELLS- MECHANISM-ACCELERATED ROS ,SUPPREESED GLUTHATIONE REDUCTASE AND DEPLETED GLUTHATIONE AND CYTOTOXICITY IN METASTATIC COLO RECTAL CANCER CELL-LoVo and LoVo/ADR[2,3,9,11,13,27,28,29,38,43 48,66,74,75,76,77,78]		

Poyphenols

PHENOLIC COMPUNDS are present and rich in black berries,23 types of wide varieties of black berries were, these were rich in anthocyanins and ellagitannins anti-oxidants ,anti-inflammatory ,anti-proliferative properties[2-41]. Identification and quantification test that is pressure liquid chromatography with photodiode array and mass spectrometry (UPLC-PDA/MS) performed showed the substances like Methyl ellagic acid pentose, Ellagitannins hex (casuarinin) Chlorogenic acid,Kaempferol-3-O-rutinoside Quercetin-3-O-pentoside Kaempferol-3-O-glucuronide Caffeoyl hexoside p-Coumaric acid Ellagitannins Lambertianin C, Apigenin-3-O-glucuronide, Ellagic acid rhamnoside Cyanidin-3-glucosylrutinoside, Luteolin-3-O-glucuronide and other compounds. Thermosensitive.[1-78]

Anthocyanins are mainly present in nature in the form of heterosides, water solubles., rich in dietary substances like berries and red grapes, red wine, cereals and purple corn, as well as some vegetables such as red cabbage. Daily consumption should range from 3 and 215 mg/day.Cardiovascular disorders can be treated. by the consumption, such as flavonal rich cocoa reduces coronary events by inducing vasodilatation (epicatechin, catechin, procyanidin oligomers). [1-78]

These are all the plant products had different properties ,helps human to boost immunity.

CONCLUSION

Flavonoids, anthocyanins, Polyphenolic amides ,Phenolic acids, Other -resveratrol in red wine and ellagic acid are rich in antioxidants ,helps in enhancing immune system, reduces oxidative stress, anti inflammatory, anti proliferative anti diabetic. So, the foods rich with this substances is used to reduce weight,sleep apnoea, prevents from cancer. chemoprevention is enhanced by these substances, improves gut, improves metabolism by inhibit amylases and glucosidase's,Ros activation, inhibition, apoptotic pathway. Further studies were required and knowledge about the substance's and dietary food enhance the life expectancy in normal and cancer patients

Recent advance broccoli consists of polysulphide -a organosulfur compounds of these veggies, glucosinolates and isothiocyanates, carry a broad spectrum of bioactivities including antioxidant activity.

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