Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 10 [8] July 2021 : 09-16

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

REVIEW ARTICLE **OPEN ACCESS**

Role of *Vitis Vinifera* as an Antioxidant Anticancer Activity

Megha Tiwari, Nikita Srivastava.
Naraina Vidyapeeth Group Of Institutions, Faculty of Pharmacy,Abdul Kalam Technical University, Kanpur,Uttar Pradesh.
Corresponding Author's Email: meghatiwari3548@gmail.com

ABSTRACT

Vitis vinifera also known as the grapevine is native to southern Europe and western Asia which belongs to the plant family of plantain family Plantaginaceae. Since ancient times, the grape has been used in folk medicine for its biological properties. Flavonoids, polyphenols, and anthocyanin are only a few of the bioactive components contained in grape seeds. The antioxidant and anti-cancer properties of grape seeds extract obtained from Narince community cultivars using various solvent mixtures were investigated. Additional methods to monitor human malignancies are needed in light of emerging developments in the occurrence of cancer of different organ sites. Various nutritive and nonnutritive phytochemicals with possible cancer chemopreventive action can be found in fruits and vegetables. Grapes and grape-based items are an example of a food component that has shown cancer chemopreventive ability while still improving overall human wellbeing

KeyWords: *flavonoids, polyphenols, anthocyanin, antioxidant, anti-cancerous, phytochemicals*

Received 14.05.2021 Revised 20.06.2021 Accepted 02.07.2021

INTRODUCTION

Vitis vinifera, the common grape vine, is a species of *Vitis*, native to the Mediterranean region, central Europe, and southwestern Asia, from Morocco and Portugal north to southern Germany and east to northern Iran [1]. Just a few *Vitis vinifera* grape varieties are commercially important for wine and table grape cultivation. There are currently between 5,000 and 10,000 varieties of *Vitis vinifera* grapes [2].

It's a flaky-barked liana that can expand up to 32 meters (35 yards) in length. The leaves are palmately lobed, alternating, and 5–20 cm (2.0–7.9 in) long and broad. The fruit is a berry known as a grape; it is 6 mm (0.24 in) in diameter in wild species and ripens dark purple or blackish with a pale wax bloom; it is far larger in cultivated plants, up to 3 cm (1.2 in) tall, and may be gray, red, or purple (black). The species is most commonly found in tropical forests and along streamsides [3].

V. vinifera subsp. sylvestris (in some classifications, Vitis sylvestris) is the wild grape, whereas V. vinifera subsp. vinifera is only found in cultivated forms. Domesticated vines have hermaphrodite flowers, but subsp. sylvestris is dioecious (male and female flowers on different plants), and fruit development needs pollination.

The grape may be consumed raw, fermented into wine or juice, or dried into raisins [4]. The majority of wines created around the world are made from *Vitis vinifera* cultivars. All of the well-known wine varieties are Vitis vinifera, which is grown on every continent except Antarctica and in many of the world's main wine regions [5].

Cancer is a public health issue that causes elevated morbidity and mortality, as well as economic and psychological difficulties. As a result, the research establishment around the globe continues to place a strong emphasis on cancer cures and prevention. "Various epidemiological studies involving various parameters such as geographical area, race, sex, age, and trans-migratory populations have collectively shown that lifestyle is one of the main influence factors in the etiology of cancer" [6]. Cancer is a term used to describe a category of diseases characterized by irregular cell growth that has the ability to infiltrate or spread to other areas of the body. Benign cancers, on the other hand, should not migrate to other areas of the body [7]. A lump, abnormal bleeding, persistent cough, sudden weight loss, and a decrease in bowel movements are also possible signs and symptoms. While these signs could suggest cancer, they could also indicate something else. Humans are affected by over 100 different forms of cancer. [8] Tobacco usage is responsible for almost 22% of cancer deaths. [9] Obesity, unhealthy

nutrition, lack of physical exercise, and heavy alcohol consumption account for the remaining 10%. Such causes include infections, ionizing radiation toxicity, and air toxins. Infections such as Helicobacter pylori, hepatitis B, hepatitis C, human papillomavirus infection, Epstein–Barr virus, and human immunodeficiency virus cause 15% of cancers in the developed world [10] [11]. These influences work by altering a cell's genes, at least in part. Until cancer may evolve, several genetic modifications are usually expected. About 5–10% of cancers are caused by hereditary mutations passed on by one's ancestors [12]. Certain signs and effects, as well as diagnostic tests, may help diagnose cancer. Medical imaging and biopsy are typically used to further examine and validate the diagnosis [13].

Many cancers may be avoided by not smoking, keeping a good weight, not consuming too much alcohol, having lots of greens, herbs, and whole grains, being vaccinated against some respiratory disorders, eliminating refined and red meat, and avoiding excessive sun exposure. [14] Cervical and colorectal cancers benefit from early diagnosis by screening. The results of breast cancer screening remain debatable [15]. Radiation treatment, anesthesia, chemotherapy, and targeted therapy are often used to cure cancer. Pain and symptom control are crucial aspects of treatment. Palliative care is especially critical for patients who are suffering from a terminal illness. The form of cancer and the nature of the condition at the time of surgery determine the chances of recovery [16]. In the developing world, the five-year survival rate for children under the age of 15 at the point of diagnosis is on average 80%. The estimated five-year survival rate for cancer in the United States is 66 percent.

In 2015, almost 90.5 million people were diagnosed with cancer. A total of 14.1 million new cases are reported per year (not including skin cancer other than melanoma). It resulted in the deaths of about 8.8 million people (15.7 percent of deaths) [17]. Lung cancer, prostate cancer, colorectal cancer, and stomach cancer are the most prevalent cancers in men. Breast cancer, colorectal cancer, lung cancer, and cervical cancer are the most prevalent cancers in women [18].

Flavonoids are a form of polyphenol found in a variety of foods and vegetables. Grape seeds are high in bioflavonoids such as resveratrol and quercetin, all of which have been shown to inhibit tumor development. Just a few of the 5,000 to 10,000 varieties of *Vitis vinifera* grapes are commercially important for wine and table grape processing.

The grapevine (Vitis vinifera) is native to southern Europe and Western Asia, but it is now produced in every climate zone on the globe. Grape seed extract and grape seed are two trade terms for sections of this plant used around the world. Furthermore, industrial and academic operations including functional foods and/or their ingredients are heavily restricted [19].

The crop, berries, and extract of grapes are already used as functional foods. Anti-inflammatory and astringent properties are found in the leaves (especially red lecccaves). A decoction of the leaves is used to cure mouth ulcers and as a douche to treat vaginal discharge. [20] a Several studies have shown that extracts of *Vitis vinifera* leaves have high antioxidant activity owing to the existence of active phytoconstituents including phenolic, flavonoids, and tannins [21].

Anthocyanins, which are responsible for the color of black, red, and purple grapes, are abundant in grapes; however, they are absent in white grapes. Anthocyanins, in particular, are often found in the skins, while procyandins are mostly in the plants [22]. The Lomanto and Colobel hybrid grape cultivars had the largest anthocyanin content (603 mg/100 g), while the Mid-south cultivar had the lowest (5.5 mg/100 g). The 3-O-glucosides of malvidin, cyanidin, delphinidin, peonidin, and petunidin are the most common anthocyanins found in grape skins. [23] In dark red vinifera grapes, malvidin, the reddest of all anthocyanins, is the most abundant, with higher proportions of cyanidin in red grapes. The main anthocyanins found in Concord grapes are cyanidin 3-monoglucoside and delphinidin 3-monoglucoside. Anthocyanins have antioxidant activity, which is thought to be a crucial biochemical feature.

ACTIVE CONSTITUENT OF *Vitis vinifera*

Flavonoids- Grape seedContains flavonoids (4-5%) including kaempferol-3-O-glucosides, quercetin-3-Oglucosides, quercetin and myricetin.

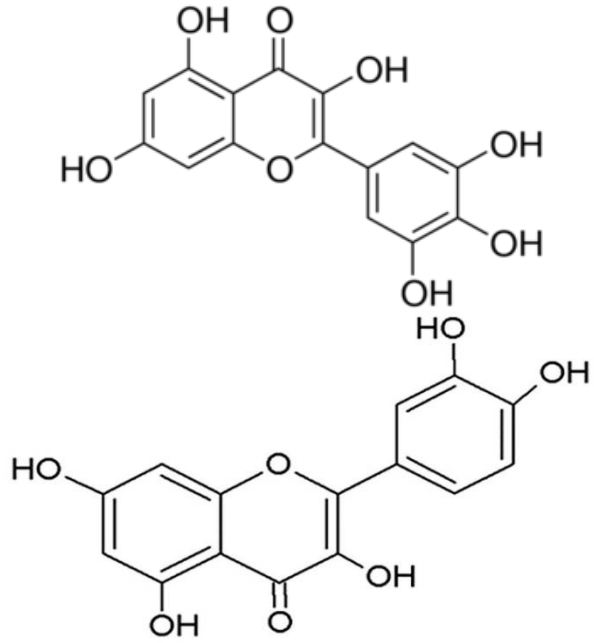
Polyphenols- Grapes are rich in polyphenols and 60– 70% of grape polyphenols are found in grape seeds. The grape seed polyphenols are flavan-3-ol derivatives. The major compounds are (+)-catechins, (−)-epicatechin, (−)-epicatechin-3-O-gallate, procyanidins dimers (B1- B5), procyanidin C1, and procyanidin.

Anthocyanins-The anthocyanins that have been reported for V. Vinifera include 3-glucosides, 3-acetylglucosides, 3-coumaroylglucosides, 3-caffeoylglucosides, 3,5- diglucosides, 3-acetyl-5-diglucosides, 3-coumaroyl-5- diglucosides, and 3-caffeoyl-5-diglucosides of cyanidin, delphinidin, peonidin, petunidin, and malvidin.

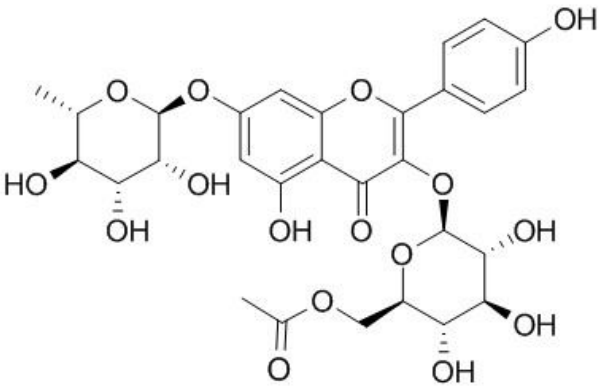
Stilbene derivatives- trans-Resveratrol (trans-3, 5, 40- trihydroxystilbene.) has also been reported in grapes.

Chemical structure of some flavonoids–

Myricetin

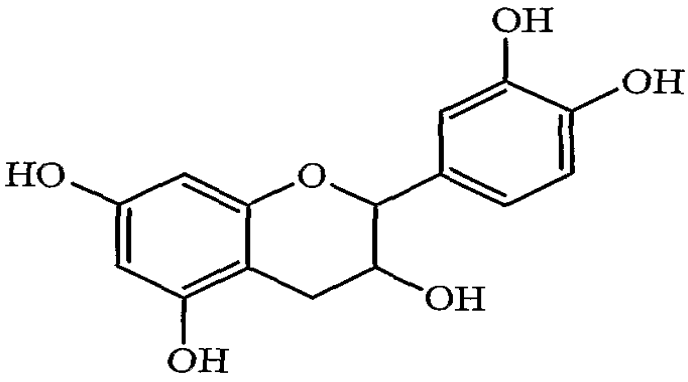


Quercitin

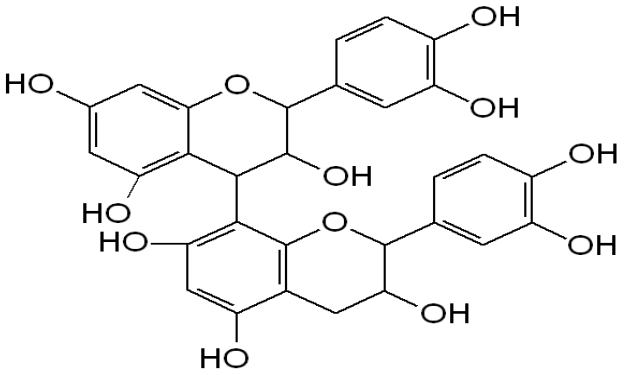


Kaempferol

Chemical structure of some polyphenols in grape seed extract-

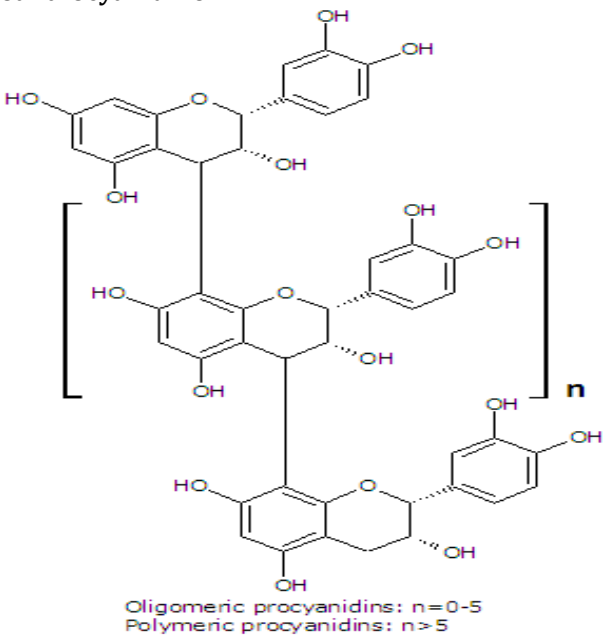


Catechin

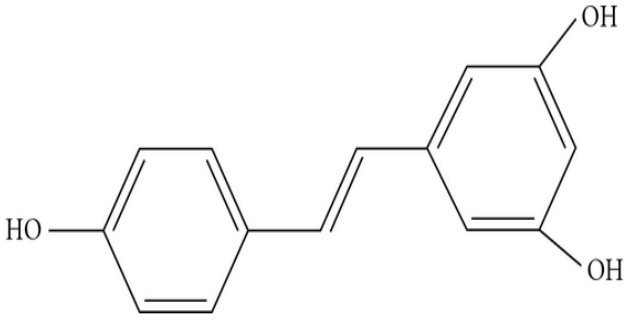


Procyanidine B1

Chemical structure of Proanthocyanidine-



Chemical structure of Stillbene derivative-



Trans resveratrol

Grape and Cluster composition –

Once the grape is ripe, the cluster composition is as follows.

Stems – Between 2% and 8% of weight.

Berries- Between 92% and 98% of weight.

Skin- Between 7% and 20% of berry weight, depending upon the grape variety. The skin holds all the components that differentiate the grape variety, like aromas, phenolic, anthocyanin and tannins.

Pulp- between 65% and 91% of berry weight. The pulp contains the sugars (sucrose and fructose) and acids (malic, tartaric, citric, succinic).

Pips – between 2% and 6% of berry weight. The pips are rich in polyphenols that in ripe grape, make a significant contribution of these compounds to the wine.

PHARMACOLOGICAL EFFECT OF *VITIS VINIFERA*-

Antioxidant activities- The antioxidant ability of human keratinocytes can be enhanced by aqueous extracts of V. vinifera L. tendrils. This impact is significant since keratinocytes that have been subjected to oxidative stress need adequate antioxidant defenses. In cardiac-derived H9c2 myocytes, lyophilized red grape juice at doses up to 0.01 g showed cardioprotective activity against doxorubicin-induced toxicity. In comparison, it increased oxidative stress in cardiac cells at concentrations of 0.01 g to 0.05 g, most likely due to pro-oxidant effects of the juice, as shown by a rise in reactive nitrogen species and antioxidant enzyme levels [25]. When considering the recommended daily intake of polyphenols for achieving an antioxidant benefit, these results should be taken into account. Furthermore, in the fruit of V. vinifera cv. Malbec, an inverse association between melatonin and malondialdehyde (MDA) levels was discovered, suggesting that melatonin is an antioxidant present in grapes.

Anticancer effect- The anticancer effects of extracts from various grape components, such as stem and seed extracts, have been studied in many experiments. In colon cancer cell lines, grape seed extract had anticancer properties and caused apoptosis. The growth inhibition caused by Italia and Palieri grape seed extracts was substantially higher than that previously observed with epigallocatechin and procyanidins [26], which is a noteworthy finding. Currant methanol extracts have cancer-preventive properties, and phenolic compounds can play a key role in this.

Grape seed extract caused apoptosis in various colorectal cancer cell lines, which was accompanied by the activation of cytochrome c in the cytoplasm and the depletion of mitochondrial membrane capacity. Intriguingly, grape seed extract not only improved the anticancer activity of 5-fluorouracil in vitro in a dose-dependent way, but it also decreased mucositis caused by 5-fluorouracil in rats following chemotherapy, with its protective effect being more noticeable in the proximal jejunum than the distal small intestine.

In addition, procyanidins in mature grape seed extract improve 5-fluorouracil's potency in human colon cancer cells. Resveratrol metabolites, such as resveratrol-3-O-sulfate, resveratrol-3-O-glucuronide, and resveratrol-4-O-glucuronide, have been shown to have anticancer effects on colon cancer cells.

They blocked the development of metastatic colon cancer cells and induced heavy cell aggregation in the S step of the cell cycle at a concentration of 30 M.

They demonstrated synergistic chemotherapeutic effects with SN38 and oxaliplatin on metastatic colon cancer cells at concentrations of 10 to 20 M. These findings are important since resveratrol metabolites may be used as a medicinal supplement to chemotherapeutic agents.

While anticancer effects of grape have been identified in cell lines and animals in laboratory trials, clinical studies on grape and its active constituents are needed to validate this action in human cancer. Since grape is such an integral part of our everyday diet, ongoing research into the importance of grape and its active components in cancer prevention is suggested[27]

Hepatoprotective effects- This influence was previously addressed in our study. Since then, several researchers have studied the effects of combining V. vinifera with other herbal medicines in various hepatotoxic models [28]. Grape and other herbs' hepatoprotective benefits seem to be due to their antioxidant, free radical scavenging, and anti-inflammatory properties. In one research, rats were given a diet containing 15% grape seed powder, which preserved many tissues, including the liver, from oxidative stress caused by 20% ethanol. It was proposed in this research that consuming functional foods may help avoid chronic degenerative liver diseases.[34]

Cardio protective effects- Oral intake of standardized grape extract (100 and 200 mg/kg) improved post-ischemic ventricular regeneration and reduced the volume of myocardial infarction. Grape seeds induced 77 percent endothelium-dependent relaxation in rat aortic rings in an ex vivo trial, while Ex Grape complete and grape seed extract (30/ml) induced 84 and 72 percent, respectively.Dietary grape seed tannins (2% monomers) have a strong antihypercholesterolemic activity due to improved reverse cholesterol transfer, as well as decreased intestinal cholesterol absorption and increased bile acid excretion. [36]

CNS effects -Grape seed extract (50 mg/kg) reduced the incidence of free-radical-induced lipid peroxidation in the central nervous system of aged rats and reduced hypoxic ischemic brain injury in neonatal rat.[37] Grape seed extract (60 mg/kg) also showed neuroprotective effects on neuronal injury induced by transient forebrain ischemia in gerbil achieved by inhibiting DNA damage. Proanthocyanidin intake (75 mg/kg, 9 weeks) was effective at up-regulating the antioxidant defense mechanism by attenuating lipid peroxidation and protein oxidation in the adult rat brain [29].

Dermatological studies-The combination GSPE (grape seed proanthocyanidine extract) containing 5000 ppm resveratrol could accelerate wound contraction and healing in mice. The application of topical GSPE facilitates oxidant induced vascular endothelial growth factor (VEGF) expression in keratinocytes by modulating pathways that are common to both H_2O_2 as well as TNF-a signaling.[39]

Antidiabetic effects- GSPE (grape seed proanthocyanidine extract) has been reported to be effective in treating diabetic nephropathy, though little is known about the functional protein changes.[40] After GSPE therapy in diabetic rats, only nine kidney proteins were found to return to normal levels. It was shown that these proteins are involved in oxidative stress, glycosylation damage, and amino acid metabolism. GPSE also ameliorated glycation-associated cardiac damage in diabetic rat.[41]

Other effects- Administration of grape seed extract, which contains 38.5% procyanidins, to hereditary cataractous rats prevented the progression of cataract formation by their anti-oxidative action.

The protective effects of a vinifera grape skin extract (200 mg/kg/day) were shown against the deleterious effects of experimental preeclampsia in rats, a condition where reduced nitric oxide production and increases in oxidative stress are present.[42] It seems that an endothelium-dependent vasodilator effect and an antioxidant action play an important role in mediating the effects of GSE in experimental preeclampsia.[43]

CLINICAL STUDIES

Effects on skin disorders. In 2010, V. vinifera extract was regarded as one of the most effective botanical ingredients for anti-aging creams [30]. A single-blinded trial of eight women (ages 45–70) in each category using one gram of trans-resveratrol (0.1 percent w/v) applied to water-in-oil (W/O) cream (10 g) alone or with -cyclodextrein (-CD). Both patients were tested on days 1 and 30 by using the creams twice a day. For all hemi-faces, both patients saw a visible change in health circumstances. Resveratrol seems to be successful in the treatment of ageing. Furthermore, combining resveratrol with -CD was more successful than resveratrol alone.The molecular processes behind this joint behavior, however, remain unknown [31]. Single-blinded randomized research on young adult stable men (n=110) was also conducted. As compared to the placebo, application of a topical water-in-oil (W/O) cream containing 2% grape seed extract on cheek skin twice a day for 8 weeks showed that the antioxidant rich formulation of grape extract has substantial effects on skin melanin levels, elasticity, and sebum material [32].anin clinical trials, a topical formulation of V. vinifera A. s-I-M.t-O.dij (Ixodermprotected women with breast cancer from the damaging impact of radiotherapy on their skin. This research suggests moisturizing the skin with a moisturizing agent like grape to shield it from the cutaneous damage induced by radiotherapy. Table 6 summarizes some of the therapeutic implications of grape and its active constituents. Toxicology is a term that refers to the presence of Resveratrol was provided to 40 healthy volunteers in four doses of 0.5, 1, 2.5, and 5 g for 29 days to study its protection and pharmacokinetic effects, as well as those of its main metabolites. The results showed that resveratrol was absolutely healthy at doses of 0.5 and 1 g, but that doses of 2.5 and 5 g had harmful gastrointestinal symptoms. The metabolites' maximum plasma amounts (CMax) and regions under the gradient (AUC) were higher than resveratrol's. It seems that resveratrol's metabolites are mostly responsible for its biochemical consequences. Resveratrol reduces the amounts of insulin-like growth factor 1 and insulin-like growth factor binding protein-3 in the blood, which may be linked to its chemopreventive properties.

Cardio protective effects- purple grape juice (7.7 1.2 ml/kg/day) increased flow-mediated vasodilation (FMD) and decreased LDL oxidation resistance in 15 adults with angiographically reported coronary artery disease (CAD). Similarly, intake of 4–8 ml/kg/day of purple grape juice for 4 weeks increased FMD of the brachial artery in patients with coronary heart disease. Purple grape juice (7 ml/kg/day) inhibited platelet aggregation, reduced superoxide release, and increased platelet-derived NO content in 20 stable subjects after 14 days of consumption. Furthermore, platelets incubated in vitro with purple grape juice generated identical effects. Furthermore, giving purple grape juice (500 mL/day) to hypercholesterolemia patients without other risk factors for 14 to 16 days increased FMD. Consumption of concentrated red grape juice (50 mL, twice a day, for two weeks) increased plasma antioxidant potential, decreased oxidized LDL concentrations, and increased cholesterol-standardized -tocopherolin concentrations in both safe subjects and hemodialysis patients.Consumption of red grape juice has resulted in a substantial decrease in plasma monocyte chemoattractant protein 1, an inflammatory biomarker linked to cardiovascular disease incidence in hemodialysis patients. Purple grape juice, on the other hand, did not seem to have any additional antithrombotic impact in patients who were still taking aspirin. Postprandial oxidative stress was reduced in healthy volunteers who drank 300 mg of a Proanthocyanidin-rich grape seed extract, by lowering oxidants and increasing antioxidant levels in plasma.As a result, LDL's tolerance to oxidative alteration has strengthened. Patients with coronary heart disease who received 600 mg of red grape polyphenol extract increased their endothelial function. 4.32

mg epicatechin, 2.72 mg catechin, 2.07 mg gallic acid, 0.9 mg trans-resveratrol, 0.47 mg rutin, 0.42 mg epsilonviniferin, 0.28 mg p-coumaric acid, 0.14 mg ferulic acid, and 0.04 mg quercetin per gram were found in grape extract. ‘‘After fasting for 30 minutes, 60 minutes, and 120 minutes, flow-mediated dilatation was assessed. “The red grape polyphenol extract caused a substantial rise in flow mediated dilatation, peaking at 60 minutes, which was slightly higher than baseline (P 0.001) and equivalent values at 60 minutes after placebo (P 0.001). “Throughout the course of the trial, there was no difference in FMD values since taking the placebo.’’

Drug Interaction-

By can intracellular doxorubicin, Ca2+, and Mg2+ concentrations thus lowering pH and mitochondrial membrane capacity, proanthocyanidin from grape seeds increased the doxorubicin-induced antitumor activity and reversed drug resistance in vitro at 12.5 and 25 mg/l and 10 mg/kg in vivo. Sarcoma 180 (S180) and Hepatoma 22 (H22) were experimentally transplanted in mice in this research. Grape juice also inhibited CYP2C9 development in vitro. Grape seed extract has been shown to have a synergistic interaction with amphotericin B in the treatment of fungal infection in mice.

Toxicity-

Acute oral toxicity, dermal toxicity, dermal irritation, and eye irritation studies have been performed with GSPE. The LD50 of GSPE was found to be greater than 5000 mg/kg when administered once orally via gastric intubation to rats.The dose-dependent chronic effects of GSPE in mice were evaluated and it was found that GPSE did not cause any detrimental effects. Furthermore, administration of the grape seed extract Activin to rats in the feed at level.″

CONCLUSION

The aim of this research was to find the most successful cancer therapy medication. One of the safest botanical additives for anti-aging creams was V. vinifera extract. “Resveratrol seems to be successful in the treatment of ageing. In women with breast cancer, a topical formulation of V. vinifera A. s-I-M.t-O.dij (Ixoderm®) has proven to defend against the damaging impact of radiotherapy on the skin. Resveratrol reduces the amounts of insulin-like growth factor 1 and insulin-like growth factor binding protein-3 in the blood, which may be linked to its chemopreventive properties. Purple grape juice (7.7 1.2 ml/kg/day) increased flow-mediated vasodilation (FMD) and decreased LDL oxidation resistance in 15 adults with angiographically reported coronary artery disease (CAD).”

Patients with coronary heart disease who received 600 mg of red grape polyphenol extract increased their endothelial function. In mice, grape seed extract and amphotericin B have a synergistic activity against fungal infection. GSPE (grape seed proanthocyanidine extract) has been shown to help diabetic nephropathy patients. Grape seed extract (60 mg/kg) also had neuroprotective effects in gerbils, preventing neuronal injury caused by transient forebrain ischemia by preventing DNA damage.

REFERENCES

1. D. Delmas, B. Jannin, M.C. Malki, N. Latruffe,(2000). Inhibitory effect of resveratrol on the proliferation of human and rat hepatic derived cell lines, Oncol. Rep. 7, 847–851.
2. M. Mouria, A.S. Gukovskaya, Y. Jung, P. Buechler, O.J. Hines, H.A. Reber, S.J. Pandol, (2002). Food-derived polyphenols inhibit pancreatic cancer growth through mitochondrial cytochrome C release and apoptosis, Int. J. Cancer 98, 76176–76179.
3. M. Kampa, A. Hatzoglou, G. Notas, A. Damianaki, E. Bakogeorgou, C. Gemetzi, et al., (2000). Wine antioxidant polyphenols inhibit the proliferation of human prostate cancer cell lines, Nutr. Cancer 37, 223–233.
4. Boyle, J. A.; Hsu, L.(1990). Identification and quantitation of ellagic acid in muscadine grape juice. Am. J. Enol. Vitic. 41, 43- 47.
5. Hanahan, D.; Weinberg, R. A. (2000). The hallmarks of cancer. Cell, 100, 57-70.
6. Lazze, M. C.; Savio, M.; Pizzala, R.; Cazzalini, O.; Perucca, P.; Scovassi, A. I.; Stivala, L. A.; Bianchi, L. (2004). Anthocyanins induce cell cycle perturbations and apoptosis in different human cell lines. Carcinogenesis, 25, 1427-1433.
7. Hotz, M. A.; Delbino, G.; Lassota, P.; Traganos, F.; Darzynkiewicz, Z. (1992). Cytostatic and cytotoxic effects of fostriecin on human promyelocytic Hl-60 and lymphocytic Molt-4 leukemic-cells. Cancer Res., 52, 1530-1535.
8. Meiers, S.; Kemeny, M.; Weyand, U.; Gastpar, R.; von Angerer, E.; Marko, D. (2001). The anthocyanidinscyanidin and delphinidin are potent inhibitors of the epidermal growth-factor receptor. J. Agric. Food Chem. 49, 958-962.
9. Manach, C.; Scalbert, A.; Morand, C.; Remesy, C.; Jimenez, L. (2004). Polyphenols: Food sources and bioavailability. Am. J. Clin. Nutr. 79, 727-747.
10. Soleas, G. J.; Diamandis, E. P.; Goldberg, D. M. (1997). Wine as a biological fluid: History, production and role in disease prevention. J. Clin. Lab. Anal. , 11, 287-313.
11. Pratt, D. E.; Hudson, B. J. F. (1990). Natural antioxidants not exploited commercially. In Food Antioxidants; Hudson, B. J. F., Ed.; Elsevier Applied Science: London, U.K., pp 171-191.

12. Soleas, G. J.; Diamandis, E. P.; Goldberg, D. M. (1997). Wine as a biological fluid: History, production and role in disease prevention. J. Clin. Lab. Anal. 11, 287-313.
13. Rice-Evans, C. A.; Miller, N. J.; Paganga, G. (1996). Structure antioxidant activity relationships of flavonoids and phenolic acids. Free Radical Biol. Med. 20, 933-956.
14. Kappus, H. (1991). Lipid peroxidations Mechanism and biological relevance. In Free Radicals and Food AdditiVes; Aruoma, O. I., Halliwell, B., Eds.; Taylor and Francis: London, U.K., pp 59-75
15. Nicholos, M. A. (1962). A spectrophotometric assay for iodide oxidation by thyroid peroxidase. Anal. Biochem. 4, 311-345.
16. Gebhardt, R.; Fausel, M. (1997). Antioxidant and hepatoprotective effects of artichoke extracts and constituents in cultured rat hepatocytes. ToxicolIn Vitro, 11, 669-672.
17. Singh, K.; Khanna, A. K.; Chander, R. (1999). Hepatoprotective activity of ellagic acid against carbon tetrachloride induced hepatotoxicity in rats. Indian J. Exp. Biol. 37, 1025-1026.
18. M.J. Wang, H.M. Huang, S.J. Hsieh, K.C. Jeng, J.S. Kuo, (2001). Resveratrol inhibits interleukin-6 production in cortical mixed glial cells under hypoxia/hypoglycemia followed by reoxygenation, J. Neuroimmunol. 112, 28–34.
19. Ames, B. N., Shigenaga, M. K., & Hagen, T. M. (1993). Oxidants, antioxidants and the degenerative diseases of aging. The Proceedings of the National Academy of Sciences of the United States, 90, 7915–7922.
20. Pezzuto, J. M. (2008). Grapes and human health: A perspective. Journal of Agricultural and Food Chemistry, 56, 6777–6784.
21. Fontecave, M., Lepoivre, M., Elleingand, E., Gerez, C., &Guittet, O. (1998). Resveratrol, a remarkable inhibitor of ribonucleotide reductase. FEBS Letters, 421, 277–279.
22. Cook, N. C., &Samman, S. (1996). Flavonoids; chemistry, metabolism, cardioprotective effects and dietary sources. The Journal of Nutritional Biochemistry, 7, 66–76.
23. Frankel, E. N., Kanner, J., German, J. B., Parks, E., & Kinsella, J. E. (1993). Inhibition of oxidation of human low-density lipoprotein by phenolic substances in red wine. Lancet, 341, 454–457.
24. Notas, G., Nifli, A.-P., Kampa, M., Vercauteren, J., Kouroumalis, E., &Castanas, E. (2006). Resveratrol exerts its antiproliferative effect on HepG2 hepatocellular carcinoma cells, by inducing cell cycle arrest, and NOS activation. BiochimicaetBiophysicaActa, 1760, 1657–1666.
25. Zhao, C.; Giusti, M. M.; Malik, M.; Moyer, M. P.; Magnuson, B. A. Effects of commercial anthocyanin-rich extracts on colonic cancer and nontumorigenic colonic cell growth. J. Agric. Food Chem. 2004, 52, 6122-6128.
26. Boyle, J. A.; Hsu, L. Identification and quantitation of ellagic acid in muscadine grape juice. Am. J. Enol. Vitic. 1990, 41, 43- 47.
27. Buege, J. A.; Aust, S. D. Microsomal lipid peroxidation. Methods Enzymol. 1978, 52, 302-310.
28. Y.L. Lin, I.M. Juan, Y.L. Chen, Y.C. Liang, J.K. Lin, Composition of polyphenols in fresh tea leaves and associations of their oxygen-radical-absorbing capacity with antiproliferative actions in fibroblast cells, J. Agric. Food Chem. 44 (1996) 1387–1394.
29. X. Tang, Z. Tian, P.-J. Chueh, S. Chen, D.M. Morre´, D.J. Morre´, Alternative splicing as the basis for specific localization of tNOX, a unique hydroquinone (NADH) oxidase, to the cancer cell surface, submitted for publication.
30. P.K. Smith, R.I. Krohn, G.T. Hermanson, A.K. Mallia, R.H. Gartner, E.K. Provenzano, et al., (1985). Measurement of protein using bicinchoninic acid, Anal. Biochem. 150 .76–85.
31. B.E. Miller, F.R. Miller, D. Wilburn, G.H. Heppner, (1987). Analysis of tumor-cell composition of tumors composed of paired mixtures of mammary tumor cell lines, Br. J. Cancer 56, 561–569.
32. H. Cutter, L.-Y. Wang, C. Kim, D.J. Morre´, D.M. Morre´, (2001). Is the cancer protective effect of green tea (K)-epigallocatechin gallate mediated through an antioxidant mechanism? Cancer Lett. 162, 149–154.

CITATION OF THIS ARTICLE

Megha Tiwari, Nikita Srivastava. Role of *Vitis Vinifera* as an Antioxidant Anticancer Activity. Bull. Env. Pharmacol. Life Sci., Vol10[8] July 2021 : 09-16