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REVIEW ARTICLE

# Review on Pharmacological Effects of Grape Seed Oil

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## ABSTRACT

**Background:** *Vitis vinifera* has been long used as herbal medicine, dietary supplement, and functional food due to its hydrophilic and lipophilic constituents. *Vitis vinifera* is commonly known as the grape vine, and many species of *Vitris vinifera* have been profusely found in the region of Mediterranean, Europe and many areas of Asia including Morocco, and Portugal.

**Objectives:** The objective of this review was to summarize the pharmacological activities of Grape Seed Oil (GSO) by analyzing various effects including anti-inflammatory, neuroprotective, anti-hyperlipidemic, anti-hepatotoxic, wound-healing effect, as antioxidant, radio-protective and hepato-protective effects.

**Methodology:** The literature was searched using Google Scholar. Initially, 53 relevant reports were shortlisted for the detailed analysis. After compiling and summarizing, 40 full-length articles were reviewed and summarized in this review.

**Results:** On basis of thorough review of 40 articles, it was found that GSO has high potential uses as nutraceutical due to its antioxidant property, total phenol and other minor constituents. Grape polyphenols have high antioxidant action; providing key role in fetus protection, while another constituent like pro-anthocyanidins have strong ability of prevention of stress-triggered abortion and resveratrol with an action on inhibition of uterine contractions.

**Conclusion:** It was concluded that GSO has numerous pharmacological activities and a very strong potential as antioxidant, anti-inflammatory, antimicrobial, neuroprotective, antihyperlipidemia, antihepatotoxic, wound-healing, radio protective and hepatoprotective. It is suggested that GSO can successfully be used as herbal medicine due to its high antioxidant potential, and phenolic compounds, grape seed oil is effective in peptic ulcer and other diseases.

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## INTRODUCTION

Vitis or grapes species belongs to family Vitaceae which is cultivated around the world and is the most important plant species[1-2]. The production of *Vitis vinifera* is about 68 million ton per annum[3-4]. Its seeds and leaves are mostly used in herbal medicine and the fruits can be used as a dietary supplements[5].

## CONSTITUENTS OF GRAPE SEED

The importance of grape seed oil as a functional food has markedly increased since 1930 due to its high hydrophilic constituents like phenol and lipophilic ingredients like tocopherol (vitamin E), phenolic compounds, unsaturated fatty acids, and phytosterol[6,7]. Grape seed oil have been used as culinary preparation because of its smell and amusing flavor and its organoleptic properties[8].

## HYDROPHILIC CONSTITUENTS

Grape seed oil is enriched with phenolic compounds like flavonoids, tannins, phenolic acids, carotenoids and stilbenes. The chief polyphenols available in the oil of grape seed includes epi-catechin, catechins, trans-resveratrol, and pro-cyanidin[9-10]. In addition to this, flavonoids have a vital impact on the action of antioxidants, therefore act as most active phytonutrients among the polyphenols having neuroprotective, cardio-protective, anti-inflammatory, antimicrobial, anti-cancer, and antiaging properties[11-12]. Moreover, flavonoids have vital impact on the action of antioxidants that helps for the removal of large amounts of simple phenolic acids. It is significantly effective in removing free radicals, influence the action of other antioxidants, and used as most potent nutraceuticals in phyto-pharmaceutical products[13]. Another important hydrophilic constituent Gallic acid, have several therapeutic actions including anti-cancer, antioxidant, antiviral, anti-inflammatory and antifungal[14-15].

## LIPOPHILIC CONSTITUENTS

Lipophilic constituents have higher percentage i.e. 85%-90% of Poly Unsaturated Fatty Acids (PUFA) that largely contain linoleic acid[16-18]. According to Kim *et al*., 2010, linoleic acid can be effective in cardio vascular disorders. Amongst Monounsaturated Fatty Acids (MUFA)[19], oleic acid is chiefly found in the oil of grape seeds, while other Saturated Fatty Acids (SFA) are existing in lesser capacities, which may vary in grapes species[20]. Grape seed oil also contain tocopherol and tocotrienol content; effective as antioxidant[21-23]. Vitamin E is also abundantly present in GSO, which makes it beneficial as neuro-protective, hepato-protective, antioxidant and stable oil[24-26]. Grape seed oils also have antiaging property[27].

## COMPOUNDS OF GSO

It has been reported that phytosterols are present in minority (Fig **1**). Where β-sitosterol is the chief ingredient of phytosterols constituent in about 67-70%[28-30].

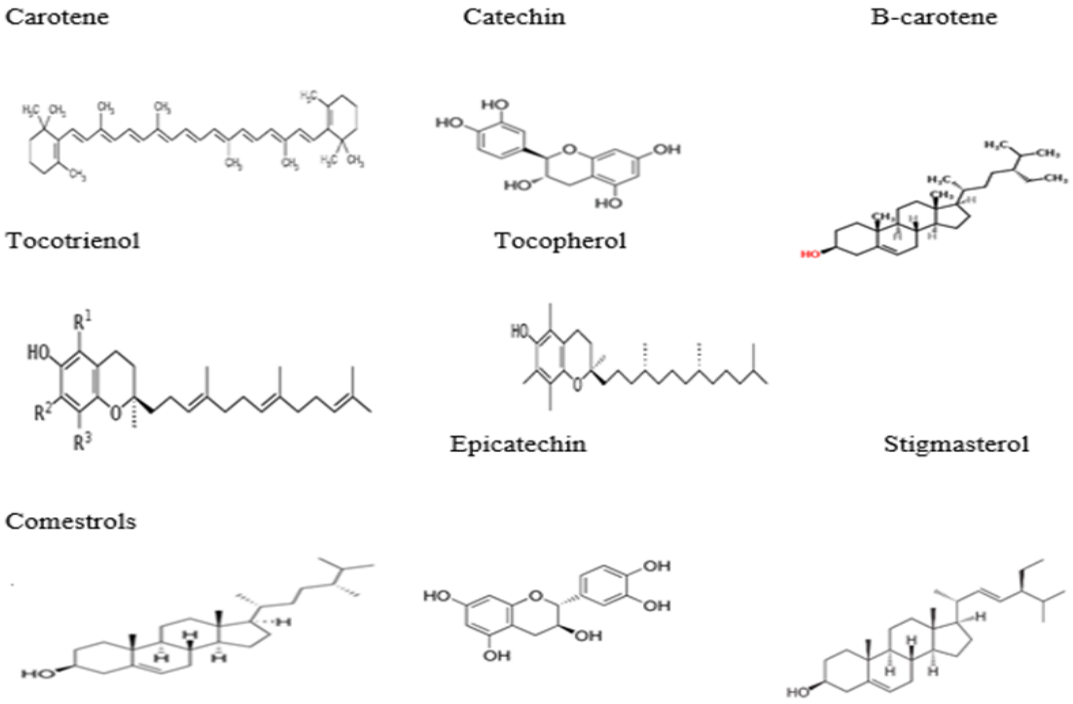


**Figure 1**. Some Minority compounds of GSO (adapted from Crews *et al*., 2006)[31].

# PHARMACOLOGICAL ACTIVITIES OF GRAPE SEED OIL

### Effect on Inflammation and Insulin Resistance

Irandoost *et al.* determined the utilization of grape seed oil in insulin resistance among females. In their study, subjects were divided in two groups; Group I was intervention group and utilized 15% energy from grape seed oil, and Group II was marked as control group and utilized 15% energy from sunflower oil with 8 weeks diet plan. Anthropometric measurements were assessed before and after the intervention. Evaluation of the results revealed that insulin resistance i.e. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR), High-Sensitivity C-Reactive Protein (HS-CRP) and TNF-α were declined in GSO treated group, hence, proved grape seed oil to be effective anti-inflammatory, with a role in insulin resistance[31].

### Neuroprotective Effect

Rubio *et al*. conducted a study to determine the useful neuroprotective effects of GSO and acute neurotoxicity induced by Carbon tetrachloride ($CCl_4$) in rats. Study results revealed major reduction in catalase, glutathione-peroxidase, and superoxide-dismutase action and also reduced the amount of glutathione. Results also revealed that prominent increase in cancer necrosis factor alpha, nitric oxide, converting growth factor-beta-1, malondialdehyde and interleukin-6. Further, rats treated with acute dose of $CCl_4$ showed increased nitric oxide synthase gene expression and xanthine oxidase. Cumulatively, this study proved that GSO have effective neuroprotective effect due to its antioxidant activity and its ability to remove the free radicals[32].

### Effect on Plasma Lipid Profile

Dae-jung *et al.* investigated the lipid profile by comparison of two oils; soya bean oil and grape seed oil and also by using lard diets. Study results revealed that rats on lard diet produced negative impact on lipoprotein metabolism by increasing body weight gain. Grape seed oil fed rats showed significant decrease in aggregate cholesterol, LDL-low density lipoprotein cholesterol, and atherogenic index, however ratio of HDL-high density lipoprotein saturated fatty acid (Cholesterol) to Total Cholesterol (TC) was significantly increased than those of soybean oil and lard groups. These results suggested that GSO supplementation has major health benefits for favorable changes in plasma lipid profiles, may provide health benefits in hyperlipidemia and other related complications compared to soybean oil and lard fed rats[33].

### Anti-Hepatotoxic Effect

Some studies showed the hepato-protective effect of GSO in rats. Hepatotoxicity was induced by $CCl_4$ and extent of hepatotoxicity was measured by biochemical parameters like aspartate aminotransferase, alkaline phosphatase, alanine aminotransferase in serum and concentrations of glutathione, superoxide dismutase, malondialdehyde, hydroperoxides, catalase and total protein in liver. This study provided the effect of grape seed oil and also compared it with vitamin E. The study results revealed that oral treatment of GSO (3.7g/kg) significantly reduced the liver enzyme Aspartate Transaminase (AST), Alanin Transaminase (ALT), and Alkaline Phosphatase (ALP) concentration in serum and increased total protein levels that indicated hepato-protective effect of GSO. The antioxidant effect of GSO was found to be similar to vitamin E (100mg/kg, orally) in Carbon tetrachloride ($CCl_4$) treated assemblies[34].

### Wound-Healing Effect

Wound therapeutic action of GSO and claret have been determined in a study by Shivananda *et al*. In their study, animals were separated into 4 groups. Group-I was topically treated with GSO and group II was treated with cranberry oil. The experimental animals were further distributed into 4 assemblies. The Group-I and Group-II study subjects were topically cured with the grape seed oil along with cranberry oil. The controls assembly (Group-III) was cured with the help of petroleum jelly. The standard group (Group-IV) was topically managed with ointment of mupirocin. The treatment capacity was evaluated by the rate of wound reduction and hydroxyl-proline amounts or ingredients. Hence, comparative analysis of the GSO and cranberry oil showed strong wound healing effect[35].

### Antioxidant Effect

Atef *et al*. conducted a study to determine the antioxidant activity of GSO in rats that exposed to diazinon (DZN) to

induce toxicity. Experimental animals were divided into 5 groups: Group I was the control group, Group II was exposed with DZN, Group III was treated with GSO and DZN, Group IV was treated only with GSO and DZN, and Group V was managed with corn oil. The extent of toxicity was determined by hemato-biochemical and histopathological alteration and progressive role of GSO. Study results revealed that Group I rats showed significant increase in blood glucose level, cholesterol , triglycerides, creatinine level, Low Density Lipoprotein (LDL), uric acid, Very Low Density Lipoprotein (VLDL), urea nitrogen, alanine amino-transferase, alkaline phosphatase, aspartate amino-transferase, lactate dehydrogenase and creatine kinase, while the level of total protein available in the blood were markedly declined. Further, histopathological consequences of the liver and kidney showed that DZN induce severe alteration in kidney, liver and testes. Group IV that was also treated with GSO did not show any alteration, thus showed protective role against toxicity induced by DZN and possible mechanism of protection. Furthermore, the current research suggested that the consequence of grape seed oil involvement against DZN harmfulness may be credited to the antioxidant part of its ingredients[36].

### Hepato-Protective Effect

Another study determined the upshot of GSO on critical liver damage induced by Carbon Tetrachloride ($CCl_4$) in rats. $CCl_4$-treated rats exhibit increase in serum aspartate transaminase activities, alanine aminotransferase and Interleukin 6 levels. Additionally, the levels of nitric oxide, malondialdehyde, nuclear factor NF-κB and the gene expression of CYP2E1 and inducible nitric oxide synthase and caspase-3 were elevated, and superoxide dismutase, catalase, glutathione peroxidase, glutathione S-transferases activities and glutathione were reduced. Additionally, trace elements alteration occurred including manganese, copper, zinc, whereas DNA fragmentation was shown in the liver tissues of the carbon tetrachloride treated group. DNA crumbling was also observed in the hepatic tissues. These properties were increased in $CCl_4$-intoxicated rats. Therefore, it was concluded that GSO exhibited protective effects because of its anti-apoptotic, anti-inflammatory and potent antioxidant action[37].

### Radio-Protective Effect

Zhenghai *et al.* determined the radio protective effect and chemical composition of grape seed oil, and the oil was analyzed by using capillary GC-MS. Grape seed oil was administered orally separately to three test mice groups with high, middle, low dose, and then the mice were exposed once to the irradiation from 60Co-γ. Results showed that the three test mice groups administered with different dosage of grape seed oil, exhibit higher recovery number of lymphocyte and white blood cell when compared with the control group, and showed significant quantity-activity relationship. Grape seed oil thus revealed good radio protective effect[38].

### Anti Hyperlipidemic Effect

Nash *et al.* proved GSO utilization to be equal to 45 grams of oil[39], which routinely showed augmented HDL and reduced LDL stages. Choi *et al.*[40] determined that grape seed oils intake in pigs reduced the levels of entire fat 30% to 20%. Kim *et al.*[41] determined plasma lipid profile in rats treated with GSO for which the results revealed prominent decline in total cholesterol and LDL-cholesterol. Asadi *et al.*[42] related that GSO supplementation produced effects on blood cholesterol and liver. Study results revealed that after 10 days, decrease in the cholesterol level was observed in rats' serum.

## CONCLUSION

In summary, GSO has numerous pharmacological activities and a very strong potential as antioxidative, anti-inflammatory, antimicrobial, neuroprotective, antihyperlipidemic, antihepatotoxic, wound-healing, radio protective and hepatoprotective. It is suggested that GSO can successfully be used as herbal medicine due to its high antioxidant potential and due to its phenolic compound grape seed oil effective in peptic ulcer and other diseases. GSO has high potential uses as nutraceutical due to its antioxidant property, total phenol and other minor constituents. Grape polyphenols have high antioxidant action, and provide key role in fetus protection. Another constituent proanthocyanidins have strong ability of prevention of stress-triggered abortion and resveratrol have action on inhibition of uterine contractions. Therefore, further investigation is required for grape seed oil individual constituents that would further show its health-promoting

properties, leading to its successful use as alternative therapy.

## CONFLICTS OF INTEREST

None.

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None.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ALP | Alkaline Phosphatase |
| ALT | Alanin Transaminase |
| AST | Aspartate Transaminase |
| DZN | Diazinon |
| GC-MS | Gass Chromatography |
| GSO | Grape Seed Oil |
| HDL | High Density Lipids |
| HOMA-IR | Homeostatic Model Assessment of Insulin Resistance. |
| LDL | Low Density Lipids |
| VLDL | Very Low Density Lipoprotein Cholesterol |

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