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REVIEW ON "GRAPE SEED EXTRACT, MORE THAN A NEUTRACEUTICAL"

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ABSTRACT

Besides being a rich for vitamins and fibre, the skin and seeds of grapes are highly rich in Polyphenols specifically proanthocyanidins, which can be used as a functional ingredient to address various health issues by boosting the natural bio-processes of the body. Antioxidant power of proanthocyanidins is 20 times greater than vitamin E and 50 times greater than vitamin C. Proanthocyanidins in Grape seeds have been shown to exhibit strong antioxidant, antimutagenic, anti-inflammatory, anticarcinogenic and antiviral activity. Through different and various studies, it was proved that the proanthocyanidin rich grape seed extract provides benefits against many diseases i.e. inflammation, cardiovascular disease, hypertension, diabetes, cancer, peptic ulcer, microbial infections, etc. Therefore, beside from using it as a nutraceutical or cosmeceutical, as a result they may have a potential to substitute or complement in currently used drugs in the treatment of diseases by developing it into other successful pharmaceutical formulations for better future prospective. This current review, disscussed about the grapeseed extract uses, its formulation into tablet dosage form and evaluation parameters.

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INTRODUCTION

Grapes are one of the most highly consumed fruits across the world. In ancient india and china the leaves and the sap of grape plants has been used in traditional treatment for ages. Besides being a wellspring for vitamins and fibre, the skin and seeds of grapes are highly rich in Polyphenols specifically proanthocyanidins, which can be used as a functional ingredient to address various health issues by boosting the natural bio-processes of the body. Since, grape seeds are by product of wine making companies therefore can be easily procured. Through different and various studies, it was proved that the proanthocyanidin rich grape seed extract provides benefits against many diseases i.e. inflammation, cardiovascular disease, hypertension, diabetes, cancer, peptic ulcer, microbial infections, etc. Therefore, beside from using it as a nutraceutical or cosmeceutical, as a result they may have a potential to substitute or complement in currently used drugs in the treatment of diseases by developing it into other successful pharmaceutical formulations for better future prospective[1].

Grape (Vitis vinifera) belongs to family Vitaceae. There are many categories of grapes with respect to their uses like wine grapes, table grapes, seedless, edible seed and raisin grapes. Seeds of grapes can be collected as a byproduct from any wine manufacturing industry. The seeds of red wine grapes are usually used to gather Grape Seed Extract (GSE)[2,3].

Fig.no.1: Vitis vinifera seeds, fruit,and seed extract.

The most common oxidants in biological systems are free radicals. Free radicals are atoms, molecules or ions with unpaired electrons that are highly unstable and active towards chemical reactions with other molecules. Free radicals are parts of groups of molecules called reactive oxygen species (ROS), reactive nitrogen species (RNS) and reactive sulphur species (RSS).

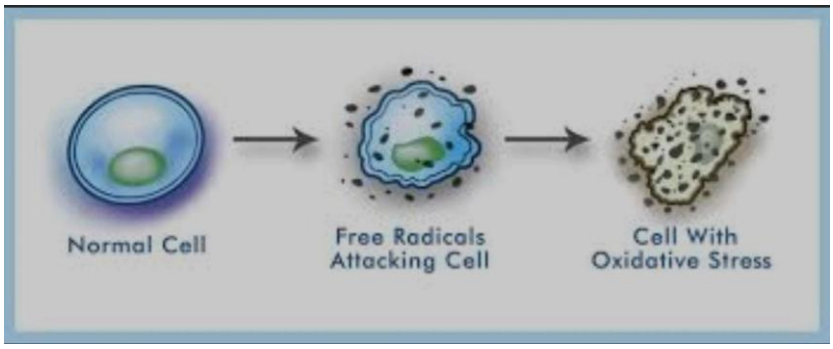

Fig.no.2: Effect of free radicals on tissue.

Free radicals can be formed in 3 ways:

- by hemolytic cleavage of covalent bond of a normal molecule, with each fragment retaining one of the paired electrons,
- by loss of Single electron from normal molecule
- by addition of a single electron to a normal molecule.

Source of free radicals:

Endogenous sources: mitochondrial leak, respiratory burst, enzyme reactions, auto oxidation reactions.
Environmental sources: cigarette smoke, pollutants, UV light, Ionizing radiation, xenobiotics.

During environmental stress and cell dysfunction, ROS levels can increase dramatically, and cause significant cellular damage in the body[4]. Thus, oxidative stress significantly contributes to the pathogenesis of inflammatory disease, cardiovascular disease, cancer, diabetes, Alzheimer's Disease, cataracts, autism and aging.

ANTIOXIDANTS AND THEIR MECHANISM OF ACTION:

Antioxidant is any substance that when present at low concentrations compared to those of an oxidizable substrate significantly delays or prevents oxidation of that substrate.

This is a broader definition encompassing many vulnerable macromolecules (e.g. DNA, lipids and proteins) that can be affected by oxidation. Up can also be defined as substances that trap harmful forms of oxygen and prevent them from damaging cells. Mechanistic.

Definitions of antioxidants are usually focused on the ability to be a hydrogen donor or an electron donor.6 Antioxidants block the process of oxidation by neutralizing free radicals. In doing so, the antioxidants themselves become oxidized. The two possible pathways are chain-breaking and preventive.7 Antioxidants are effective because they are willing to give up their own electrons to free radicals. When a free radical gains the electron from an antioxidant it no longer needs to attack the cell and the chain reaction of oxidation is broken. After donating an electron an antioxidant becomes a free radical by definition. Antioxidants in this state are not harmful because they have the ability to accommodate the change in electrons without becoming reactive.

BENEFITS OF HERBAL ANTIOXIDANTS OVER THE SYNTHETIC ANTIOXIDANTS[5]:

- Can reduce blood pressure.
- Can improve blood flow.
- Could reduce oxidative damage.
- May improve collagen levels and bone strength.
- Supports your brain as it ages.
- Can improve kidney function.
- Can inhibit infectious growth.
- May reduce cancer risk.

Antioxidant power of proanthocyanidins is 20 times greater than vitamin E and 50 times greater than vitamin C. Proanthocyanidins in grape seeds have been shown to exhibit strong antioxidant, antimutagenic, antiinflammatory, anticarcinogenic and antiviral activity and scavenge reactive oxygen and nitrogen species, modulate immune function and platelet activation, and produce vasorelaxation by inducing nitric oxide (NO) release from endothelium.

Phytochemical Compounds in Grape Seeds

Grape seeds contain protein (11%), fiber (35%), minerals (3%), and water (7%). In addition, the lipid content of grape seeds ranges from 7 to 20% .The oil content of grape seeds is traditionally extraction using mechanical methods or organic solvents. In mechanical extraction, although the quality of product is superior, the extraction gives a lower yield. While organic solvent extraction gives a higher yield, it requires solvent recovery through distillation and the final product contains traces of residual solvent. While the supercritical method is regarded as a promising method which can produce similar quantity and better quality of oil yield than mechanical and organic solvent extractions. Cold-pressing is used to extract the oil from grape seeds without chemical treatment or heat. Although the cold pressing usually gives a lower yield than other conventional solvent extraction, it may retain more bioactive components and be safer because there are no solvent residues in the grape seed oil. Several studies have been conducted on grape seeds, in order to determine their bioactive compounds. Grape seed extracts contain a heterogeneous mixture of monomers (5 30%), oligomers (17–63%), and polymers (11–39%) composed of proanthocyanidins. Proanthocyanidins are the major compound in grape seed extracts. The red color and astringent taste of grape seed extracts can be attributed to proanthocyanidins. However, higher concentrations of proanthocyanidins may affect the sensory and color properties of the product[6,7].

FORMULATION AND EVALUATION OF GSE TABLETS[8]:

Precompressional Evaluation Study of BLENDS:-

Bulk density:

The bulk density was measured by using cylinder and measuring the volume and weight.

Tapped density:

Tapped density was determined by placing a graduated cylinder containing a known mass of drug on a mechanical tapper apparatus which was operated at fixed number of taps until the powder bed volume had reached to minimum. The unit of tapped density and untapped density is reported in g/ml. Bulk density was calculated using the following formula.

Bulk density=weight of the powder/ Bulk volume of powder

Tapped density =weight of the powder /tapped volume of powder

Compressibility index:

The interparticulate interactions influencing the bulking properties of a powder are also the interactions that interfere with powder flow, a comparison of the bulk and tapped densities can give a measure of the relative importance of these interactions in a given powder. Such a comparison is often used as an index of the ability of the powder to flow, for example the Compressibility index or Hausner's ratio.

Relationship between % compressibility and flow ability.

% compressbility	flow ability
5-15	Excellent
12-16	Good
18-21	Fair to passable
23-35	Poor
33-38	Very poor
>40	Extremely poor

Formula for % compressibility index:

$$\% \text{ compressibility index} = [1 - V/V0\ ] \times 100$$

Where, V and Voare the volumes of the sample after and before the standard tapping respectively

Formulation of GSE Tablets:-

Preparation of mixed blend of drug and excipients-

All the ingredients were passed through mesh no. 60. Required quantity of ingredients was weighed as given in Table and coground in mortar and pestle. The powder blend was evaluated for flow property and compressibility behavior.

Compression of GSETablets-

Grape seed extract tablets were prepared by direct compression method using various formulation additives in varying concentrations and the detailed composition was shown in the Table 2. All the ingredients were powdered separately in a clean and dry porcelain mortar and then they were passed through # 60 mesh sieve. The drug and the additives were mixed thoroughly in an inflated polyethylene pouch in a geometric ratio of their weight. Then the powder mixture was compressed in to tablets of 300 mg weight using 6 mm flat round punches.

Ingredient
Grape seed extract
Diluent
Binder
Direct compressible vehicle
Glident & lubricant

Evaluation of GSE Tablets:-

Tablet thickness and size:-

Thickness and diameter of tablets were important for uniformity of tablet size. Thickness and diameter was measured using Vernier Callipers**.**

Hardness:-

Hardness exhibits tensile strength of tablet. The force needed to fracture the tablet by diametric compression is referred as crushing strength of tablet. Hardness is a deformation property of solid. The hardness of the six tablets from each formulation batch was determined using Monsanto hardness tester.

Friability:-

Friability is the measure of tablet strength. Roche type friabilator was used for testing the friability using the following procedure. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm dropping the tablets through a distance of six inches with each revolution. After 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.

Formula for friability-

% loss = initial weight of tablets-finial weight of tablets/initial weight of tablets x 100

Uniformity of weight[10]:-

Standard values for uniformity of weight:

Average weight of Tablet (mg)/ IP/BP	Maximum percentage of deviation allowed (%)
80 or less	10
80-250	7.5
More than 250	5

Twenty tablets were taken and their weight was determined individually and collectively using single pan electronicbalance. The average weight of the tablets was determined from collective weight. From the individual tablet weight, the range and percentage deviation was calculated Not more than 2 tablets should deviate from the average weight of tablet and maximum percentage of deviation allowed.

Disintegration study-

In the disintegration time study, six tablets were tested. Each tablet was put into 900 ml HCL solution (0.1N) at 37 ± 2^{0}C. Time required for complete dispersion of a tablet was measured with the help of disintegration test device.

Dissolution Study-

All the tablet dissolution studies were carried out for three tablets (triplicate) per formulation. USP Type II dissolution apparatus was used for drug release studies. Parameters were used in release study

- Speed of paddle
- Temperature
- Sampling time
- Volume drawn
- Dilution factor
- Volume of dissolution medium
- Dissolution medium
- Spectrophotometric analysis
- UV-Visible at 280 nm

1, 1-diphenyl-2-picrylhydrazyl (DPPH) Radical scavenging activity:-

An Aliquot of 3ml of 0.004% DPPH solution in methanol and 0.1 ml of plant extract at various concentrations (20, 40, 60, 80, 100, 120, 140, 160, 180 and 200ug/ml) were mixed. The mixture was shaken vigorously and allowed to reach a steady state at room temperature for 30 minutes. Decolorization of DPPH was determined by measuring the absorbance at 517nm. A control was prepared using 0.1 ml of respective vehicle in the place of plant extract/ ascorbic acid. The %inhibition activity was calculated by using the following formula.

Formula for DPPH activity-

%inhibition= absorbance of control-absorbance of GSE/ absorbance of ascorbic acid *100

absorbance of control

CONCLUSION

Therfore from this articeit was conclued that from using GSE as a nutraceutical or cosmeceutical, as a result they may have a potential to substitute or complement in currently used drugs in the treatment of diseases by developing it into other successful pharmaceutical formulations for better future prospective.

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