Abstract:
Going natural is an option which is always considered unanimously the best in combating diseases especially chronic inflammatory diseases. Other than drugs these components can be easily included under diet supplements, thus decreasing the apprehension and increasing compliance of the patient and are free from side effects. Grape seed extract (GSE) possesses an array of compounds which prevent chronic inflammatory diseases, by scavenging free radicals, inhibiting collagenases, histamine etc, disrupting plaque and improving immunity. Time has come to shift the treatment paradigm from blind eradication of bacteria by chemotherapy to modify the aggregation, neutralizing by-products and enhancing mucosal immunity of host using natural products.

Keywords: bioflavonoids, vitis-vinifera, proanthocyanidin.

HISTORY AND CHEMISTRY:
Grape botanically known as Vitis vinifera has been used as an integral part of diet dating back to centuries. In late nineteen century Jacques Masquelier a French biochemist reported that seed of grapes which are generally discarded as useless waste instead contain high concentration of certain bioflavonoids including catechins, epicatechin, and epicatechin-3-O-gallate. Later Dr. Masquelier's developed a French prescription drug, known as Endotelon for the treatment of venous insufficiency and other disorders of the vascular integument. Recently St. Leger et al; Renaud and De Lorgeril, in an epidemiological data have shown that red wine may reduce the mortality rate from coronary heart disease, the so-called "French paradox". Since then ongoing researches and controlled trials have been directed to find its application in the field of dentistry.

Vitis vinifera seeds include catechin and epicatechin monomers, dimers of Catechin and epicatechin, known as leucoanthocyanidin, or proanthocyanidin B1, B2, B3, and B4 in free and esterified form with gallic acid, trimers and tetramers of catechin and epicatechin. They also constitute of oligomers of various combinations of flavon units of 5 or more catechin and epicatechin monomers, trace amounts of tannins and hydroxycinnamic acids, including caffeic acid, p-coumeric acid, and ferulic acid.

MECHANISM OF ACTION
Antioxidant property: Grape seed have been proposed as potent antioxidant which are 20 times more efficient than vitamin C and 50 times than vitamin D. Gallic acid found in grape seeds has strong antioxidant activity; it has been reported as one of the most potent scavenger of oxygen free radicals. Shakagami et al demonstrated synergetic effect of Gallic acid with vitamin C, thus enhancing each other's antioxidant and cytotoxic effects. Maffie et al reported Proanthocyanidin to scavenge superoxide, hydroxyl, and hydrogen peroxide as well as lipid peroxide radicals, in a dose dependent manner.

ANTI-INFLAMMATORY PROPERTY:
Proanthocyanidins inhibit extracellular and interstitial collagenase, thereby reducing collagen degradation as well as progression of Periodontitis. It also possess hyaluronidase inhibiting activity which maintain integrity of the matrix. It suppress lipopolysacchride induced matrix metalloproteinase (MMP) secretion by macrophages and inhibit human MMP-1 and MMP-9 activities. Serine proteases are known to activate the salivary and gingival interstitial collagenase. Which are inhibited by proanthocyanidins thereby decreasing collagenase enzyme.

Catechin monomers block the excessive production of histamine by inhibiting histidine Decarboxylase, while assisting in reducing the excessive release of neutrophilic lysosomal enzymes, collagenase and serine protease. Proanthocyanidins efficiently restrain the inflammatory response of activated neutrophils in vitro and whenever absorbed in vivo can prevent their oxidative discharge at the site(s) of their adhesion. Thus all these factor contribute to decrease cardinal signs of inflammation decreasing edema, erythema and pain.

IMPROVING CONNECTIVE TISSUE PROFILE:
Proanthocyanidins have selective affinity for connective tissue of the body. They Strengthen and protect collagen and elastin fibers found in the periodontium, as well as the skin, heart, blood vessels, joints, mucous membranes, and cell membranes.
INHIBITION OF BACTERIA.

Gall acid has been shown to inhibit the protease activity of periodontopathogenic bacteria which includes three strains of Bacteroides gingivalis and Bacteroides intermedius and two strains of Treponema denticola. These findings also suggest that gall acid may interfere with the virulence and growth of periodontopathogenic bacteria[11].

Proanthocyanidins binds to the polymeric filament surrounding bacterial cell membranes, preventing there co-aggregation (a crucial step in plaque biofilm formation) and hence formation of plaque which being fundamental etiology of periodontal diseases [12]. Polyphenols also have been reported to inhibit streptococcus mutants and prevent dental caries.[13]

IMMUNITY MODULATION & OTHERS:

Flavonoids exert significant immunomodulatory effects by differentially regulating the production of Th1 cytokines, via induction of Interferon gamma.[14] Grape seed extract (GSE) have been reported to be active against HIV by inhibiting virus expression and replication.[15] It Enhances bone density and encourages wound healing by vascular endothelial growth factor release in experimental animals. [16,17] GSE decreases tumor numbers and reduces the malignancy of papillomas, protect against carcinogenesis and provide supplementation for sunscreen protection. Resveratrol (a polyphenol in grape seed) may interfere with cancer cell growth and proliferation, as well as induce apoptosis. [18-20]

SAFETY CONCERNS:

The grape seed extract (GSE) has been examined for acute / subchronic oral toxicity and mutagenicity. No evidences were reported at dosages of 2 and 4 g/kg of body weight in rodents. Side effects most often include headache, dizziness or nausea with a dry, itchy scalp. Interactions between grape seed extract and medicines/other supplements have not been carefully studied. Due to characteristic of limiting platelet adhesion grape seed extract may increase the clotting time of blood.[21]

The US National Centre for Complementary and Alternative Medicine (NCCAM) reports that oral administration of grape seed extract was well tolerated in people over 8 weeks of a clinical trial.[22] GSE is considered safe for oral administration and potentially free of side effects and termed GRAS (generally regarded as safe) [23]

CONCLUSION:

Grape seed extract (GSE) possess a promising hope for treating chronic inflammatory diseases like Periodontitis, rheumatic arthritis etc... in a more natural rational and safer way.

In periodontal context GSE can be used as a adjunct to conventional treatment gold standards i.e scaling and root planning or as an independent treatment approach. More longitudinal data and vigorous randomized controlled trials based on clinical signs and pocket depth evaluation are needed to evaluate and understand the mechanism and functions of bioflavonoids.

REFERENCES:

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Table no 1. Functional properties of GSE and related studies.

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