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Study on Anti-Ulcerative Property of *Solanum nigrum* Polyphenols

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ABSTRACT

Blackberry Nightshade (*Solanum nigrum*) is a species of flowering plant in the **Solanaceae** family, it is a natural medicinal plant. Its berries and leaves are mainly medicinal and have many therapeutic effects. The whole plant is medicinal in nature and is used as an antiseptic, anti-inflammatory, digestive, diuretic, etc The main aim of the study is to investigate the Anti-ulcerative effect of polyphenols found in Solanum leaves, such as gallic acid. nigrum plant in Wistar rats. We hypothesized that the polyphenols in the leaves of the SN plant could reduce gastric secretion. However, Solanum Nigrum polyphenols can be used in the treatment of gastric ulcers by reducing gastric secretion in the stomach.as we have explored, a peptic ulcer occurs when stomach acid eats through the lining that protects the stomach and causes an open ulcer. Typical signs and symptoms are burning abdominal pain and indigestion. Ulcers are common and treatable, but if left untreated for too long, they can become serious. Some ulcers bleed continuously, which can cause significant blood loss over time. Some may continue to eat through the stomach until a hole forms. The most common causes of ulcers are the use of over-the-counter pain relievers and the widespread H. pyroli bacterial infection. Because of the complexity and chronicity of gastric ulcers, animal models are relied upon to mimic human disease.

INTRODUCTION

The topic or study is based on the Anti-ulcerative effect of solanum nigrum polyphenols on gastric ulcer, because gastric ulcer is a serious problem with a mortality rate of about 10% for leaky peptic ulcers.

Peptic ulcer disease is characterized by damage to the gastrointestinal (GI) mucosa due to secretion of stomach acid or pepsin. It extends to the muscularis propria layer of the gastric epithelium. It usually occurs in the stomach and proximal duodenum. This may involve the lower esophagus, distal duodenum, or jejunum. This activity examines the causes, pathophysiology and presentation of ulcer disease and emphasizes the role of professional groups in its management.[1]

Peptic ulcer disease (PUD) occurs when someone develops ulcers in the stomach or upper small intestine. Ulcers affect about 4 million Americans.

Ulcers occur when excess acid breaks down the mucous membrane. This increased risk of acid damage may be due to a bacterial infection or other causes such as genetics, over-the-counter pain relievers such as NSAIDs, alcohol consumption or smoking.

It extends to the muscularis propria layer of the gastric epithelium. It usually occurs in the stomach and proximal duodenum. Peptic ulcer disease (PUD) is a worldwide problem with a lifetime risk of 5 to 10 percent. Overall, the incidence of PUD has decreased worldwide due to improved sanitation and hygiene and effective treatment and judicious use of NSAIDs. Duodenal ulcers are four times more common than stomach ulcers. In addition, duodenal ulcers are more common in men than in women. About half of the world's population is infected with the H-bacterium. pylori (often without symptoms). H. pylori causes about half of all stomach ulcers in the world. Pain associated with a peptic ulcer often occurs within 2-3 hours after eating. Peptic ulcers are diagnosed more often in women than in men. Furthermore, the ASIR is calculated in the same way for both male and female patients. At the same time, a significant negative correlation was observed between EAPC and ASIR ($R = -0.29$, p.

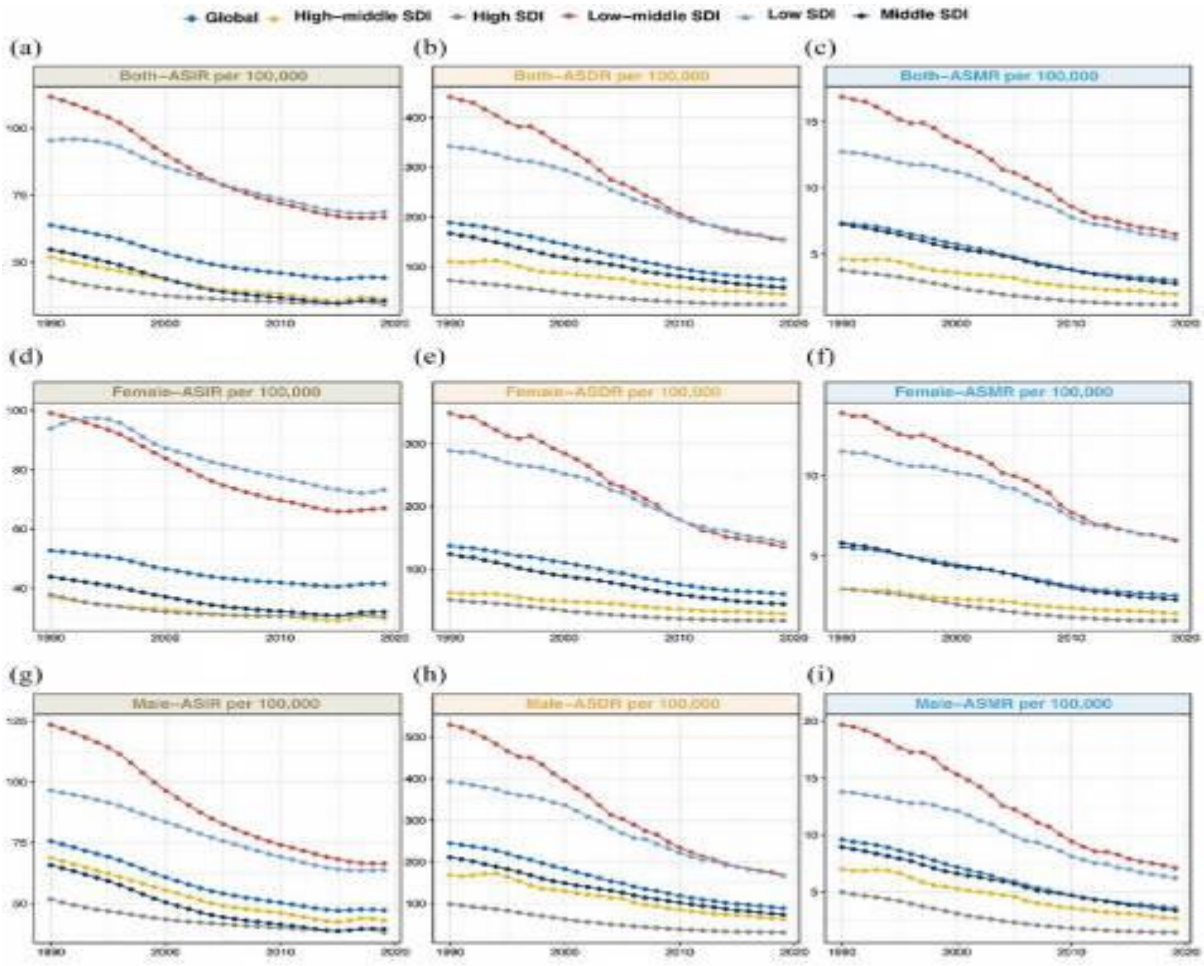

Figure 1:Trends of changes in ASIR, ASDR, ASMR between different SDI countries. (a, d, g) ASIR; (b,e,h) ASDR; (c, f, i) ASMR.

ASDR, cost DALY by age; ASIR, age-standardized incidence rate; ASMR, age-adjusted mortality ratio; SDI, Sociodemographic Index.[2]

This makes the topic more important to discuss, and compared to other herbs, Solanum nigrum is cheap and readily available.

The next study involves Wistar rats because they mimic the human digestive system and can develop stomach ulcers in a very short period of time. This makes them an idol in research.

Ulcers were induced by a single oral dose of indomethacin (30 mg/kg body weight). Wistar rats were pretreated with esomeprazole (reference drug) at a dose of 20 mg/kg body weight.[3]

Black nightshade (*Solanum nigrum*) is a medicinal plant belonging to the Solanaceae family. Native to Eurasia and introduced to America, Australasia and South Africa. This plant is found in many forest and disturbed habitats. The height is 30-120 cm, the leaves are 4.0-7.5 cm long and 2-5 cm wide. It is often used in folk medicine for the treatment of many diseases due to its bioactive principles, including glycoalkaloids, glycoproteins, polysaccharides, etc.

Solanum nigrum belongs to the Solanaceae family commonly known as black nightshade or garden nightshade in English. Ganikesopu in Kannada, Makoya in Hindi, Munatakali in Tamil, Kachchipandu in Telugu, and Bengali in Gudakam [4]. Solanum nigrum, an annual plant, has dull, dim green leaves that are delicious, applauded or lanceolate, and innocuous or slightly toothed [5]. Extra axillary pendulous umbral cells with 3-8 flowers [6]. Ripe fruits are thin and black [7]. It has antimicrobial, antioxidant, cytotoxic, antiulcer and chemopreventive properties. In Africa, this herb has been used to treat various fatal diseases in children, including febrile seizures, visual disturbances, hydrophobia and chronic autoimmune diseases. It is a potential herbal alternative with anticancer properties [8].

Figure 2: *Solanum nigrum*

Taxonomical classification [10]	**Synonym**[9]
Kingdom: Plantae Class: Magnoliopsida Division: Magnoliophyta Family: Solanaceae Order: solanales Genus: *Solanum*-nightshade Species: *Solanum nigrum*	Hindi: Makoya Kingdom: Plantae English: Black nightshade Class: Magnoliopsida Sanskrit: Dhvansamaci Division : Magnoliophyta Kannada: Ganikesopu Family: Solanaceae Bengali: Gudakamai Order: Solanales Malayalam : Manatakkali Genus: Solanum-nightshade Marathi: Kamoni

Polyphenols such as gallic acid, catechin, protocatechinic acid and caffeic acid, epicatechin and rutin are found in leaf extracts, which have desirable anti ulcerative effects and can be used to treat or reduce the symptoms of gastric ulcers.

Gastric ulcers are most often found in the lesser curvature, while duodenal ulcers are found in the bulb of the duodenum. The wound is round or oval and the base is smooth. Acute ulcers have regular borders, while chronic ulcers have raised borders with inflammation. The wound extends beyond the muscularis mucosa.[1]

In peptic ulcers, there is usually mucosal damage extending to the muscularis mucosa. When the protective superficial mucosal layer is damaged, the inner layers are sensitive to acidity. In addition, the ability of mucosal cells to excrete bicarbonate is at risk.

H. pylori is known to colonize the gastric mucosa and cause inflammation. B. pylori also impairs bicarbonate secretion, which contributes to acidity and gastric metaplasia.[1]

This plant has many other functions such as antioxidant, anti-inflammatory, hepatoprotective, diuretic and antipyretic etc.

There are a couple of valuable review papers addressing the pathogenesis of gastric ulcer.

The order in which the topic will be discussed are as follows:-

1. Gastric ulcers as a chronic & complex disease.

2. Scope & role of polyphenols in Gastric ulcers.

3. Method of extraction of polyphenols from the solanum nigrum plant.

BODY

1. Gastric ulcers as a chronic & complex disease.

A peptic ulcer is a break in the stomach mucosa that penetrates the muscular mucosa and reaches a diameter of more than 5 mm. The body has natural ways of protecting the stomach lining from the harmful acidic environment that is the stomach lumen. When there are changes in the defense mechanisms of the stomach, it can cause changes in the lining of the stomach, which eventually leads to erosion and then ulcers. This activity explores the assessment and management of peptic ulcers and explains the role of the interprofessional team in improving the care of patients with this condition. [11]

It is important to understand that this disease process is both preventable and treatable. The stomach lining is protected by prostaglandins, mucous membranes, growth factors and proper circulation. Smoking, hydrochloric acid, ischemia, NSAIDs, hypoxia, alcohol, and Helicobacter pylori infection are known damaging factors to this barrier.

Symptoms-:

- Burning stomach pain
- Feeling of fullness, bloating or belching
- Intolerance to fatty foods
- Heartburn
- Nausea

Less often, ulcers may cause severe signs or symptoms such as:

- Vomiting or vomiting blood — which may appear red or black
- Dark blood in stools, or stools that are black or tarry
- Trouble breathing
- Feeling faint

- Nausea or vomiting
- Unexplained weight loss
- Appetite changes

Pathophysiology of Gastric Ulcer

The mechanism of peptic ulcer disease (PUD) results from an imbalance between protective and destructive factors in the gastric mucosa. Risk factors for PUD:

• H. pylori infection

• NSAID use

• First-degree relative with PUD

• Immigrant from a developed country

• African-American/Hispanic[1]

The pathophysiology of MU is multifactorial and not yet fully understood. Although the exact cause is unclear, a number of possible mechanisms have been proposed. One of the main culprits is the presence of highly acidic gastric secretions, which have been associated with gastrojejunostomy (GJ) ulcers in Billroth procedures involving parietal cell-rich gastric segments [12]. After RYGB, antral stimulation and gastrin release are reduced as food bypasses the antrum. However, the gastric mucosa is able to respond to vagal and hormonal stimuli that maintain an acidic environment [13]. The jejunal mucosa, which lacks protective buffering mechanisms, is sensitive to the effects of gastric secretions [14]. Local activation of pepsin in the jejunal mucosa is thought to be due to the high acidity of gastric secretions, leading to the formation of MU [15]. In addition, gastric fistula formation after RYGB has been found to lower gastric pH. This occurs when residual gastric acid flows through the fistula into the pouch, contributing to the development of MU [17, 16]. Several other possible risk factors, such as comorbidities (diabetes, H. pylori) and lifestyle factors (smoking, use of anti-inflammatory drugs, alcohol consumption) reduce tissue perfusion and cause local ischemia and chronic inflammation. In addition, the use of serotonin reuptake inhibitors (SSRIs) has been associated with an increased risk of ulcer bleeding. This may be due to the anticoagulant

effects of SSRIs and their potential ulcerative effect on the intestinal mucosa, which may affect platelet function and increase the likelihood of bleeding.

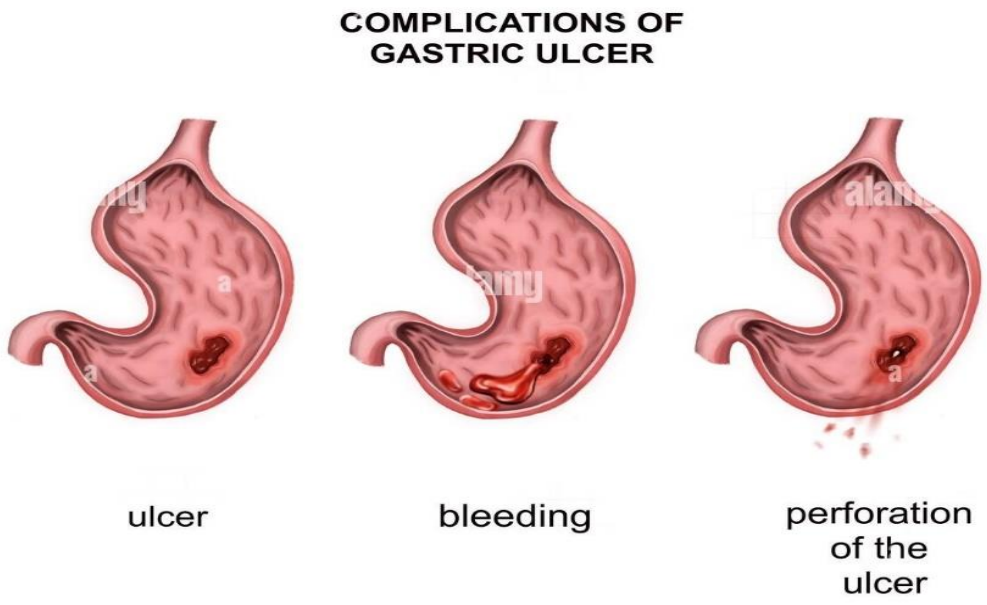

Figure 3:Complications of gastric ulcer

2). Scope & role of polyphenols in Gastric ulcers.

Polyphenols represent a group of chemical substances common in plants, which are structurally characterized by one or more phenolic units. Polyphenols are the most abundant antioxidants in the human diet, and the largest and best studied class of polyphenols are the flavonoids, which contain several thousand compounds. Numerous studies confirm that they protect human health and are key elements of a healthy and balanced diet. Epidemiological studies correlate the consumption of flavonoids with a reduction in the incidence of chronic diseases such as cardiovascular disease, diabetes and cancer. The involvement of reactive oxygen species (ROS) in the etiology of these degenerative conditions suggested that phytochemicals with antioxidant activity may contribute to the prevention of these pathologies. This review discusses phenolic compounds in plants and reports recent studies. In addition, previously presented work provides information on the relationship between the dietary intake of these compounds and the risk of disease, i.e., the impact on human health. Results on herbs and essential oils from tropical, subtropical and temperate plants have also been reported.

Phenolic compounds, or polyphenols, form one of the most numerous and widespread groups of substances in the plant kingdom, and currently more than 8,000 phenolic structures are known [18]. Phenolic compounds vary in structure from simple molecules such as phenolic acids to highly polymerized compounds such as proanthocyanidins (tannins) found in plants and common in many foods (fruits, vegetables, cereals) and beverages (wine, beer). , you do) [19]. The most common phenols in human food are phenolic acids, flavonoids and tannins [20]. Phenolic compounds have at least one aromatic ring with one or more hydroxyl groups and can be classified as flavonoids and non-flavonoids [21].

Based on their basic chemical structure, polyphenols can be divided into at least 10 different categories. Flavonoids are one of the most important groups and can be divided into 13 different classes in which more than 5000 compounds have been described. In recent years, interest in polyphenols and other antioxidant molecules has increased among agricultural and food scientists, nutritionists, food specialists and consumers [18].

Polyphenols provide health benefits through several mechanisms, such as free radical scavenging, protection and renewal of other dietary antioxidants such as vitamin E, and chelation of prooxidant metals. In mainly esterified or glycosylated plants, the nature and concentration of phenolics varies dramatically [22]. They have beneficial properties such as antioxidants, immune-modulating effects, and anticancer and antibacterial effects. Some studies have shown that these phytochemicals improve wound healing [23].

Based on previous reports, polyphenols and their metabolites with strong anti-inflammatory, antioxidant, anticancer and immunomodulatory properties may be promising candidates for the treatment of various gastrointestinal diseases such as gastritis, stomach cancer, colon cancer, IBD and IBS. Since polyphenols can positively modulate the bacterial population of the gut microbiome, they can help regulate the host's immune system and thus improve overall gut health [24,25,26]. Similarly, Kim and coworkers [27] reported that polyphenols and their active metabolites increased the production of SCFAs and BCAAs and may be useful in the treatment and prevention of various gastrointestinal disorders such as Crohn's disease, ulcerative colitis, and colon and rectal cancer. Metabolic syndrome by preventing inflammation and oxidative stress. In addition, the authors wish to emphasize the gastroprotective property of polyphenols and therefore this review only deals with the mechanism related to gastrointestinal cancer, especially gastric and colon cancer. Since the pathophysiology of different gastrointestinal diseases is different (as mentioned above), the

mechanism of treatment of these gastrointestinal diseases by polyphenol would be multidirectional, so the authors compiled all the main possible mechanisms (signaling pathway, curcumin) for each polyphenol (green tea). polyphenol). Resveratrol, quercetin) based on various cell lines and animal studies and strong clinical evidence.

Structure of some polyphenols

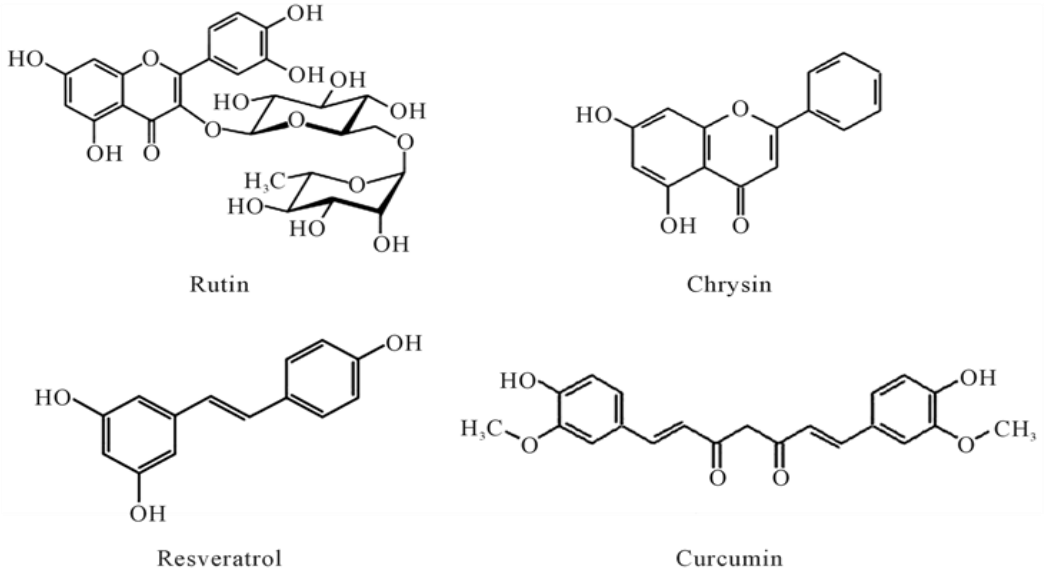

Figure 4- Structure of some polyphenols

POLYPHENOLS AS NATURAL ANTIOXIDANT

Most of these substances are classified as natural antioxidants, indicating their importance in oxidative stress. A number of synthetic phenolic antioxidants such as butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), tert-butylhydroquinone (TBHQ), 2-tert-butyl-4-methylphenol (TBMP) and gallic acid are currently used in the food industry. esters, e.g. propyl gallate (PG). These synthetic antioxidants are considered harmful to human health. High doses of TBHQ cause negative health effects in laboratory animals, such as DNA damage, which can lead to stomach tumors [28]. BHA has been reported to act as a tumor promoter and tumor promoter in some animal tissues [29].

Phenolic compounds (Figure 4), like other antioxidants, are generally used to reduce the harmful effects of substances with high oxidation potential. The antioxidant properties of polyphenols are mainly due to their redox properties, which enable them to act as reducing agents, hydrogen donors and singlet oxygen quenchers [30].

Among compounds with an oxidizing effect, i.e. reactive oxygen compounds are superoxide radical ( ), hydrogen peroxide (H2O2), hydroxyl radical (OH•) and singlet oxygen (1O2) [31].

Phenolic Compounds and Free Radicals

Elimination of free radicals is not favorable in normal physiological conditions due to their low concentration. Therefore, the primary defense against these species, and thus the end of radical chain reactions, depends on the action of substances known as antioxidants. These compounds reduce free radicals and reactive species, preventing damage to cellular structures and oxidative degradation. When constantly exposed to high concentrations, the system that repairs these harmful substances (antioxidants) cannot keep up with the demand, leading to the accumulation of reactive substances, which causes so-called oxidative stress. Oxidative stress is therefore an imbalance between the production of oxygen species and the defense system provided by antioxidants, which causes cell damage and is directly related to chronic degenerative pathology, as described in several reports [32]–[35] . Free radicals are produced naturally in the body through several metabolic reactions, such as mitochondrial respiration and enzymatic oxidations catalyzed by oxidases. Thus, enzymatic antioxidant defense systems including oxidoreductases such as superoxide dismutases (SOD), peroxidases (POD), catalase (CAT) and glutathione peroxidase (GPx) are active to minimize the harmful effects of free radicals.

Polyphenols and inflammation

The immune-modulating effect of polyphenols is supported by various studies: some polyphenols influence immune cell populations, modulate cytokine production and the expression of pro-inflammatory genes [36, 37]. For example, the cardioprotective effect of resveratrol found in red grapes and nuts was mainly due to its anti-inflammatory properties. In vivo and in vitro studies show that resveratrol can inhibit COX, inactivate peroxisome proliferator-activated receptor gamma (PPARγ), and induce eNOS (endothelial nitric oxide synthase) in mouse and rat macrophages [38, 39, 40]. Similarly, the resveratrol analog RVSA40 inhibited the proinflammatory cytokines TNF-α (tumor necrosis factor alpha) and IL-6 (interleukin-6) in RAW macrophage 264.7 macrophages. Another example is the nonflavonoid curcumin, which is found in turmeric and mustard. Curcumin has been shown to decrease the expression of inflammatory cytokines: TNF and IL-1, adhesion molecules such as ICAM-1 (intrinsic adhesion molecule-1) and VCAM-1 (vascular cell adhesion

molecule-1) in human umbilical vein. endothelial cells and inflammatory mediators such as prostaglandins and leukotrienes. It also inhibits certain inflammation-related enzymes such as COX (cyclooxygenase) in mice, LOX (lipoxygenase) in human endothelial cells, MAPK (mitogen-activated protein kinase), and IKK (inhibitor of kappa kinase). In addition, curcumin inhibits NF-κB (enhancer of nuclear factor kappa light chain of activated B cells) and STAT3 (signal transducer and activator of transcription) and reduces expression of TLR-2 (toll-like receptor-2). and 4, while in vivo it increases PPARγ (peroxisome proliferator-activated receptor gamma) in adult male rats [41, 42, 43, 44, 45, 46]. Caffeic acid phenethyl ester inhibited TLR4 activation and LPS-mediated NF-κB in macrophages, and quercetin has also been shown to inhibit leukotriene biosynthesis in human polymorphonuclear leukocytes [47,48] . COX2 expression is also reduced in colon cancer cells and androgen-independent human prostate cancer PC-3 cells by ECGC (epigallo-catechin gallate), gingerol en, and piceatannol (an analogue of EGCG found in spruce), leading to NFk B inactivation.[38]In addition, polyphenols such as Gingerol and Quercetin can activate the production of adiponectin, which is known for its anti-inflammatory effects [49,50]. EGCG also inhibits NFKB activation in human epithelial cells and reduces expression of iNOS (inducible nitric oxide synthase), NO (nitric oxide) production in macrophages, leading to its immunomodulation [51, 52, 53] Several in vitro studies have shown that other polyphenols, such as oleanolic acid, curcumin, kaempferol-3-O-sophoroside, EGCG and lycopene, inhibit the high-mobility group box1 protein, an important chromatin protein that interacts with nucleosomes, transcription factors, and histones. Regulates transcription and plays a key role in inflammation. All these examples support the anti-inflammatory effects of polyphenols.

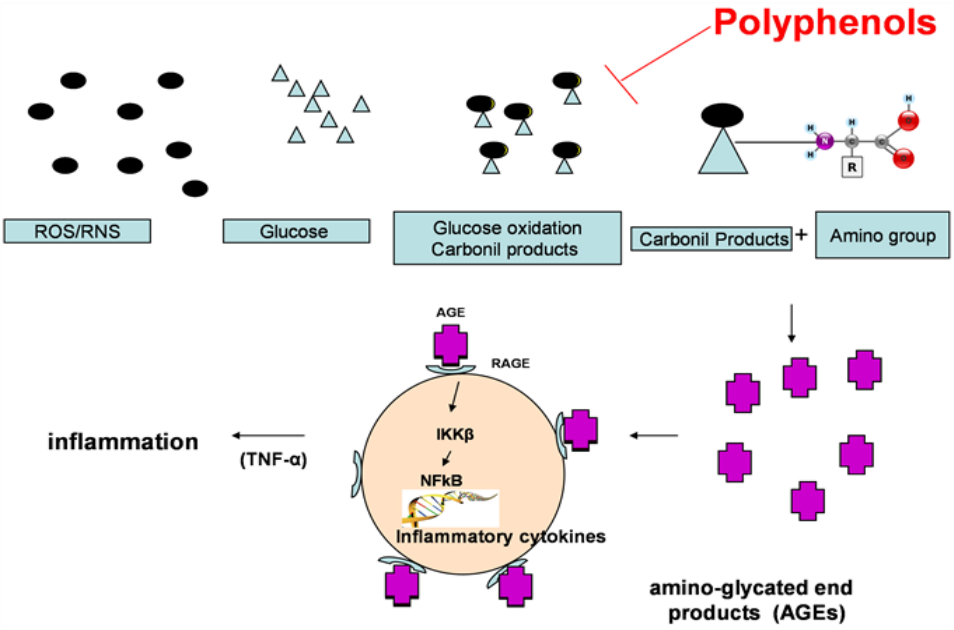

Figure-5: effect of polyphenols on inflammation

3)-Method of extraction of polyphenols from solanum nigrum.

Extracting polyphenols from Solanum nigrum (black nightshade) involves several methods, typically using solvents to separate the polyphenolic compounds from the plant material. Here's a general outline of the extraction process:

Materials Needed:

1. **Black nightshade** (*Solanum nigrum*) plant material (leaves, berries, or whole plant)
2. **Solvent**: Ethanol, methanol, or a mixture of water and organic solvents (like ethanol)
3. **Grinder or blender**
4. **Filter paper or mesh**
5. **Separatory funnel or centrifuge (optional)**

Extraction Procedure:

1. **Preparation of Plant Material**:

- Collect fresh Solanum nigrum plant parts (leaves or berries) and clean them thoroughly to remove dirt and contaminants.

- Dry the plant material if fresh material is not available. However, fresh material is generally preferred for higher polyphenol content.

2. **Grinding/Blending**:

- Grind the cleaned and dried plant material into a fine powder using a grinder or blender. This increases the surface area and facilitates better extraction of polyphenols.

3. **Extraction**:

- **Cold Extraction**: Place the powdered plant material in a suitable container (like a glass jar) and cover it with a solvent (ethanol, methanol, or a solvent mixture).

  - Seal the container and let it stand for a period (hours to days), shaking occasionally. This allows the polyphenols to dissolve into the solvent.

- **Hot Extraction**: Alternatively, heat the solvent and plant material mixture under controlled conditions (usually below boiling point of the solvent) for a specified time to accelerate extraction. However, excessive heat may degrade sensitive polyphenols.

4. **Filtration**:

- After extraction, filter the solvent-extract mixture to separate the liquid extract from the solid plant debris. Use filter paper or a fine mesh to achieve this.

5. **Concentration**:

- Concentrate the polyphenol-containing extract using techniques like rotary evaporation or simple evaporation under reduced pressure and controlled temperature. This step removes the solvent and leaves behind a concentrated polyphenol extract.

6. **Purification (Optional)**:

- If needed, further purify the extract using techniques such as column chromatography or liquid-liquid extraction to isolate specific polyphenolic compounds.

7. **Storage**:

- Store the purified extract in a cool, dark place in amber-colored glass containers to protect it from light and oxidation, which can degrade polyphenols.

Notes:

- **Solvent Choice**: Ethanol and methanol are commonly used because they effectively extract a wide range of polyphenols. Ethanol is safer for handling and less toxic compared to methanol.

- **Safety**: Work in a well-ventilated area when using organic solvents, and follow safety guidelines for handling chemicals.

By following these steps, you can effectively extract polyphenols from Solanum nigrum for various research or industrial purposes. Adjustments to the method may be necessary based on specific research goals and the characteristics of the polyphenols of interest.

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