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Original Review Article

ROLE OF GREEN TEA WITH APPLICATIONS, BENEFICIAL EFFECTS, ITS POTENTIAL HEALTH IMPLICATIONS AND ACTIVE CONSTITUENTS IN COSMETICS

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Abstract

Tea is one of the most widely consumed beverages worldwide, and is available in various forms. As compared to other forms of tea, Green tea is richer in antioxidants. The health benefits of green tea for a wide variety of ailments, including different types of cancer, heart disease, and liver disease, were reported. Currently, tea extracts, due to their rich composition and various biological actions, play an important role among the dietary supplements and cosmetics. Green tea (GT) extracts contain polyphenols, known to be effective free radical scavengers, and other ingredients that could also provide benefits to the skin.

Keyword:- caffeine, matcha, catechin, epicatechin, epicatechin-3-gallate, epigallocatechin, epigallocatechin gallate

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INTRODUCTION

1. What is green tea?

Camellia sinensis is a species of evergreen shrubs or small trees in the flowering plant belonging to family Theaceae whose leaves and leaf buds are used to produce tea[1]. Although green tea is grown from a single plant, slight variations in tea processing (usually in the way the tea is rolled) have created a number of varieties of green tea. Popular green tea varieties include Gunpowder, Hyson, Dragonwell, Sencha, and Matcha[2]. Within the last decade cosmetics market continues to grow globally. The growth of the upper middle class, an increasing number of senior citizens around the world and the expansion of online beauty spending and social networks, which certainly set new trends among the consumers, are all having an impact on an increasing interest in skin care products. Natural products as the cosmetics' ingredients are often associated with safety, marked activity and good quality. That is why a great interest can be observed in cosmetic products of natural origin[3].

- Green tea shows various activities which are listed as follows-

i. Anti-carcinogenic property- The cancer-protective effects of green tea have been reported in several population-based studies. For example, cancer rates tend to be low in countries such as Japan where green tea is regularly consumed. It is not

possible to determine from these population-based studies whether green tea actually prevents cancer in people. However, emerging animal and clinical studies are beginning to suggest that EGCG may play an important role in the prevention of cancer. It has been suggested that EGCG and other tea catechins suppress tumour growth by inhibiting the release of tumour necrosis factor-alpha, which is believed to stimulate tumour promotion and progression of initiated cells as well as pre-malignant cells[4].

ii. Antioxidant property- Green tea enhances humoral and cell-mediated immunities, decreasing the risk of certain cancers and cardiovascular diseases. Much of the cancer chemopreventive properties of green tea are mediated by EGCG and it has been assumed that it induces apoptosis and promotes cell growth arrest by altering the expression of cell cycle regulatory proteins. EGCG is a valuable scavenger of reactive oxygen species (ROS), such as superoxide radical, singlet oxygen, hydroxyl radical, peroxyl radical, and peroxynitrite; is important in promoting carcinogenesis; and has strong antioxidant activity. It protects cellular damage by inhibiting DNA damage and the oxidation of low-density lipoprotein (LDL) and many putative health benefits of tea are presumed to be caused by its antioxidant effects[5]. In a study done by Atsumi et al. (2007), consumption of green tea increased the free radical scavenging activity (FRSA) ($P < 0.05$)[6].

iii. Antibacterial effect- GTCs inhibit the growth of various bacteria, showing their antibacterial effects. Recently, a comparative study revealed that the minimal inhibitory concentration of EGCG was much lower than that of EC and that EGCG caused more intensive damage of the membranes compared with EC, indicating the importance of a galloyl moiety for the effects of catechins. Catechins and green tea extracts show minimal inhibitory concentrations ranging 100-1,000 Mmol/L against various bacteria. In an oral pharmacokinetic study, catechins were found to maintain the Mmol/L concentrations in human saliva after oral application of green tea extracts. At the corresponding concentration levels, all the eight catechins reduced membrane fluidity[7].

iv. Antiviral properties- Tea catechins show a defending effect against human immunodeficiency virus (HIV)[8,9]. Kawai et al. studied the mechanism of the anti-HIV effect of green tea polyphenols and stated that EGCg (but not ECG) straight binds to the cell-surface CD4 molecules[10].

- PREPARATION OF GREEN TEA

Step 1-Green tea is prepared by exposing the freshly collected leaves to the air until most of the moisture is removed.

Step 2-Then they are roasted and stirred continuously until leaves become moist and flaccid.

Step 3-Then they are passed to rolling table and rolled into balls and subjected to a pressure which removes the moisture.

Step 4-Then the leaves are shaken out on the copper pans and roasted again till the leaves assume dull green colour.

Step 5-Then the leaves are winnowed, screened and graded into various varieties[11].

2. Role of green tea-

Green tea (GT) extracts contain polyphenols, known to be effective free radical scavengers, and other ingredients that could also provide benefits to the skin. The results suggest that Green tea containing cosmetic formulations have pronounced moisturizing effects and improve skin microrelief [12].

Tea plant itself and its extracts together with their centuries-old tradition of use play an important role on the cosmetics market. In general, cosmetics products containing tea extracts rich in polyphenols

have a positive effect on the skin appearance and ameliorate skin damage, erythema and lipid peroxidation following UV exposure[13].

Green tea has always been considered by the Chinese and Japanese as a potent medicine for the maintenance of health, endowed with the power to prolong life [14].

3. Active constituents of green tea -

Green tea mainly constitutes polyphenols, caffeine, amino acids and other nitrogenous compounds, vitamins, inorganic elements, carbohydrate and lipids. The infusion mainly constitutes polyphenols, caffeine, theanine, vitamin etc. Carbohydrate is the major constituent of tea leaf that includes cellulosic fiber and the next is protein, but these components are not soluble.

i. Polyphenol:

Tea polyphenols are generally infused with sizzling water or can be extracted with ethyl acetate. The taste of green tea is bitter and astringent due to polyphenol content. The green tea mainly constitute 6 kinds of catechin: (-)-EGCG is found in larger amount and next to this are (-)-EGC,(-)-ECg, (-)-EC are found in decreasing order. Minor components are (+)-GC and (+)-C. Catechins (-)-ECG and (-)-EGCG are ester type and are stronger in bitterness and possess astringent effect more than (-)-EC and (-)-EGC [15]. Catechin synthesis is done in tea leaves using malonic acid-and shikimic acidmetabolic pathways. During shikimic acid-metabolic pathway an intermediary product is formed and gallic acid is derived from that. A number of papers have been published on the antimutagenic activity, suppressive effect of chromosome aberration, antioxidant activity, depressor effect on renal hypertension, inhibitory effects on arteriosclerosis of green tea polyphenols.

ii. Caffeine:

Caffeine is mainly a trimethyl derivative of purine 2, 6-diol and is produced from leaves of the tea plant from the ancient time. Coffee beans contain about 1.5 % caffeine, while caffeine content of green tea is up to 5%. It functions as a cardiac and also as a diuretic. It can also stimulate the cerebral cortex which results in central nervous system excitation. But, for certain people it is the cause for irritation in the gastrointestinal tract and sleeplessness.

iii. Amino acids and other nitrogenous compounds:

Among total nitrogen found in the green tea infusion, one fifth of them originate from caffeine and related compounds. Other forms of nitrogenous compounds found in tea infusion are amino acids, amides, certain proteins, and nucleic acids. During tea manufacturing most of the proteins are bounded with tannins that make them insoluble. The total nitrogen content in the green tea extracts is 4.5 to 6.0 %, and free amino acids constitute half of it. Major amino acids found in the green tea infusion are Theanine and glutamic acid, and next to that aspartic acid and arginine are found. The amino acid content is found to be more in spring harvested tea leaves than harvested in other seasons.

iv. Vitamins:

Commercially available green tea is rich in Vitamin C (VC, ascorbic acid) and contains near around 280 mg in 100 g dried leaves whereas oo-long tea and black tea contain less vitamin C because they undergo fermentation process.

v. Inorganic elements:

In green tea leaves aluminium and fluorine content are found to be more as compared to other plants. It is shown that fluorine has preventive effect against dental caries and this exists as anion form in tea leaves. A number of fluorine compounds are produced by Fluoride anion, they prevent bacterial attack to teeth by covering the surface. Roasted tea at high temperature contains aluminium fluoride complex but not effective against dental caries.

vi. Carbohydrates:

Green tea contains near about 40% total carbohydrate and cellulosic fiber constitute one third of it. Green tea quality is affected by starch. Starch synthesis starts at dawn and finish with sunset. Therefore starch content in tea leaves significantly varies in a day. Tea harvested in afternoon content more starch as compared to harvested in morning but tea harvested in morning found to be better in terms of quality.

vii. Lipid:

Oil content of tea leaves is about 4 % by weight. The tea oil is non-drying, and its solidifying temperature is -5 to 15 ºC[16].

viii. Flavonoids:

Flavonoids comprise a group of secondary plant constituents widespread in nature that are available from dietary sources such as cocoa, green tea, soy, berries, or other fruits[17]. Flavonoid containing phytomedicals are used as antiinflammatory and antiallergic remedies and a flavonoid-rich diet is suggested to play a role in the prevention of several kinds of cancer and cardiovascular disorders18. Many of the alleged effects have been linked to the antioxidant properties of flavonoids; however, they also exhibit other biological activities[18]. In a study of high- and low-flavanol cocoa products, ingestion of cocoa dietary flavanols contributed to endogenous photoprotection and improved dermal blood circulation[19,20].

4. Potential health implications of green tea-

i. Cancer-

Many studies suggest an inverse relationship between green tea intake and the risk of variety of cancers, although other studies have found no association. Clinical trials have been small and heterogenous with contradictory results. Dietary, environmental, and population differences may account for these consistencies.

A 2006 meta-analysis of epidemiologic studies found that high intake of green tea was associated with a 20% reduction in the risk of breast cancer (odds ratio [OR]= 0.78; 95% confidence interval [CI], 0.61 TO 0.98)[21].

Green Tea Polyphenols (GTP), particularly EGCG or EGCg (epigallocatechin gallate) not only inhibit an enzyme required for cancer cell growth, but also kills cancer cells with no ill effect on healthy cells. A team of scientists at Purdue University determined: “In the presence of EGCg, the cancer cells literally failed to grow or enlarge after division then presumably because they did not reach the minimum size needed to divide they underwent programmed cell death, or apoptosis.” Although not all studies gave positive result about green tea inhibiting or preventing growth of cancer cells[22].

ii. Against Candidiasis-

The green tea polyphenols significantly decreased the ability of C. albicans to grow and sustain biofilms. Further investigation on the possible effects that these polyphenols had on C. albicans metabolism implicated proteasome involvement. The tea catechins may also affect other metabolic pathways besides proteasome disruption in C. albicans, preventing the normal signals for growth and development of biofilm infections[23].

iii. Against pulpitis-

Many types of cytokines and adhesion molecules are responsible for the initiation and progression of pulpitis. Dental pulp cells (a major cell type in the dental pulp) also have the capacity to produce proinflammatory cytokines, such as IL-6 and IL-8, and express adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) in response to inflammatory stimuli, including the

bacterial component. In the present study, the authors showed that the catechins EGCG and ECG inhibit the expression of proinflammatory cytokines and adhesion molecules in human dental pulp cells (HDPC) treated with LPS and peptidoglycan (PG). These findings suggest that GTCs may arrest the exacerbation of pulpal inflammation[24].

iv. Against leukoplakia-

In a double-blind intervention trial performed by a group from Beijing in China, 29 out of 59 patients with oral leukoplakia were randomized to use a mixed tea extract orally as well as a topical tea extract. After the 6-month trial, the oral lesions had decreased in size in almost 40% of the patients treated, which was associated with a decrease in proliferation in the treatment group on histopathologic examination ($P < 0.05$)[25].

v. Blocking of DNA Synthesis-

EGCG has an antiinflammatory effect by elevating the expression of the Tollip protein, a negative regulator of TLR signaling[26]. GTPs also prevent tumor progression of chemically induced benign skin papillomas to carcinomas, probably by stabilizing DNA and protecting against free radical-mediated enhancement of genetic instability[27].

Green tea with its components has been shown to interact with multiple cellular mechanisms, giving rise to several potential health implications[28].

vi. Effect of EGCG on the proteasome-

The proteasome is responsible for the degradation of more than 90 % of intracellular proteins. By this mechanism, the proteasome regulates turnover of cyclins and cyclin-dependent kinase inhibitors (CIP/KIP family). Consequently, the inhibition of proteasome functions can result in cell cycle arrest and proves crucial for cell survival and proliferation. In cancer cells, this homeostatic function is deregulated by cellular oncogenic factors leading to hyperactivation of the proteasome. Increased proteasome activity in turn promotes the degradation of tumor suppressor proteins, resulting in cancer cell survival and proliferation as well as the development of drug resistance. As a consequence, proteasome inhibitors have been repeatedly suggested for anticancer treatment, and are currently being tested in (pre-)clinical trials. EGCG has been shown to block the proteasome, potentially indicating an antitumor effect of green tea[29].

vii. Effects on growth factor-associated signaling-

Epidermal growth factor (EGF) is a general growth factor with action not only on epithelial cells but also on a large variety of other cells, accounting for disparate cellular activities such as proliferation, angiogenesis, survival, differentiation, migration, and apoptosis[30]. Today, it has been established that there is an epidermal growth factor receptor tyrosine kinase (RTK) family, which is currently extensively studied for its role in human development, physiology, and cancer[31]. EGCG and other GTPs have been shown to interact with epidermal growth factor-associated signaling by inhibiting EGFR autophosphorylation in carcinoma cells[32]. Moreover, EGCG can inhibit cell transformation by directly interacting with cellular target proteins such as the SH2 domain of Fyn tyrosine kinases[33]. Targeted disruption of the EGF receptor has been shown to block the development of papillomas and carcinomas from human papillomavirus-immortalized keratinocytes[34], which could in part account for the chemopreventive and antipapillomatous activity of topically applied EGCG.

EGCG has also been shown to block other growth factors such as platelet derived growth factor (PDGF)35, fibroblast growth factor (FGF)[36], vascular endothelial

growth factor (VEGF), and insulin-like growth factors (IGF-1 and IGF-2)[37]. Interactions of EGCG with growth factor-associated signaling have been shown to be in part due to the inhibition of intracellular signaling cascades but also due to "trapping of growth factors" by EGCG[36].

5. Beneficial effects of green tea-

i. Gargling effect-

Gargling with a catechin extract of green tea-inhibited influenza infection and application of green tea extract to the oral or nasal cavities suppressed various pathogenic bacteria[38].

Mouthwash/Gargles which contains a green tea solution, an anti-inflammatory, natural, and harmless substance, can reduce the pain of sore throat in patients after endotracheal extubation[39]. Green tea is a natural, anti-microbial, and harmless substance that can reduce the prevalence of sore throat. Drinking green tea prevents getting sore throats and colds since it helps fight the bacteria harboring in the throat and various researches have been carried out that explore the effect of green tea gargling on sore throat caused by intubation in patients after CABG surgery. The results showed that green tea gargling was effective against sore throat 12 and 24 hours after removal of endotracheal tubes[40].

To prevent the infection of the flu, gargling with diluted green tea is advised. Warm tea is effective and first or second serve of tea is effective because it contains more catechins[41].

Green tea can be used as adjuvant to oral hygiene maintenance with a goal on the prevalence of periodontal diseases due to its antibacterial and antioxidant properties. Dental plaque is the major etiologic agent for the initiation of gingivitis[42]. Gingival disease can progress to periodontitis which if left untreated may eventually compromise the entire periodontium.The most abundant components in green tea are phosphoenol in particular, flavonoids such as the catechins43. Mouthwashes were equally effective in reducing plaque and gingival inflammation, considering the fact that the chemical formulations of commercially available mouth rinses are synthetic based, expensive, and have considerable side effects, which restricts their use[44].

ii. Anti-Cellulite and Slimming Properties-

Cellulite (gynoid lipodystrophy), often called 'orange peel effect', is a typical women's ailment, which mainly appears on the thighs and buttocks[45]. Green tea, due to the content of alkaloids, is widely used in the production of cosmetics against cellulite. The major one—caffeine (known also as theine) stimulates microcirculation in the skin, which in turn improves cell oxygenation and accelerates fat burning in skin cells. Therefore, cosmetic preparations containing alcoholic or glycolic tea extracts are used to maintain a slim figure, reduce cellulite and remove toxic products from the body. Not only alkaloids, but also polyphenols, are very effective in reducing cellulite. Catechins, which are a dominant compounds present in tea extracts, were described to inhibit glycation and oxidation of proteins and thus preventing the formation of cellulite, which is one of the symptoms of skin aging. Therefore, tea is a common ingredient in cosmetic preparations with firming, slimming and anti-cellulite properties[46-48].

Rao and co-investigators tested a cream containing green tea, caffeine, black pepper, sweet orange peel, ginger root extract, cinnamon bark extract and capsaicin. The formulation was applied under occlusion with neoprene shorts to 20 patients. After testing 76% of the volunteers noticed an overall improvement of their cellulite, with 54% reporting greater improvement in the thigh that received garment occlusion. Professional

dermatological examination revealed significant improvement of the skin of the thighs condition (average circumference reduction was 1.2 cm; 1.3 cm in the group with occlusion and a 1.1 cm reduction without occlusion)[49]. Although there are many cosmetic preparations for the treatment of cellulite, which contain different tea extracts, the literature review showed almost no studies evaluating the effectiveness of tea polyphenols in the treatment of cellulite. Their efficacy towards cellulite reduction is mostly based on their properties to treat obesity, decrease weight, reduce waist circumference and improve thermogenesis [50,51].

iii. Neutralizes free radicals-

EGCG is a powerful antioxidant and key polyphenol that can be found in green tea, and acts as an effective defence against free radicals.

So, what are free radicals exactly? Well, they are molecules that already exist within our body and surroundings, but external influencers such as smoke, smog, pollution and UV exposure changes their makeup, eventually mutating them into something harmful.

In today's modern world, we are all exposed to more pollution than before, which is why we need to do what we can to safeguard against them, including applying moisturizer. By having too many free radicals, their effect on the body can begin to manifest, resulting in accelerated signs of aging and cell degradation. By using green tea moisturizer, you can help block the UV and pollution enter your body, resulting in better overall health.

Moisturizes dry skin-

Green tea moisturizer is normally non-greasy, but can still have strong moisturizing benefits on dry skin, without over-moisturizing skin that is naturally more oily. The best part is, that you'll know that what you put on your skin will be completely natural, with very little scope for side-effects. If you have a dry skin type, green tea moisturizer should be applied alone or under makeup[52].

iv. Prevent Dark Circles-

Who has been plagued by dark circles and puffiness in their lifetime? Green tea, other than being rich in antioxidants, also contains tannin and caffeine. When applied topically to the eye area, they can remedy this problem of dark circles and puffiness. This is primarily because they shrink the fine blood vessels around the eyes, making for a great undereye fix. Take two freshly brewed and used green tea bags for this, put them in the fridge for an hour, take them out and place them on your eyes. Leave on for 10-15 minutes, then remove. You'll feel instantly refreshed. The question that sometimes arises is - why green tea over black, which also contains tannin and caffeine? Green tea also contains flavonoids, which offer benefits to reducing the appearance of fine lines below the eyes, and making sure the undereye area stays youthful and firm for as long as possible. Additionally, green tea contains lutein and zeaxanthin, which promote eye health, keeping ailments like glaucoma and cataract at bay[53]. (also we can use a roll on of green tea with aloe vera and cucumber to prevent dark circles)

6. Applications of green tea-

i. In tooth decay -

Tea is a herbal substance with anticaries property; the inhibitory effect of green tea on tooth decay has been reported. As per the result of a study done by Naderi et al. shows that Iranian green tea has an inhibitory effect on streptococcus mutans54. (Splat toothpaste with green tea protects against tooth decay and prevents gum disease.)

Mechanism of action:-

Step 1- Effect on cariogenic enzyme

The streptococcal glucosyl transferase degrades the dietary sucrose and

synthesizes extra and intracellular polysaccharides[55,56]. hese polysaccharides help in adherence of bacteria to the tooth surface, formation of plaque biofilm and generate energy during reduced availability of exogenous fermentable carbohydrates in the oral cavity.Green tea has a constituent named epigallocatechin-3-gallate(EGCG) which suppresses the salivary and bacterial amylases involved in carbohydrate metabolism. It prevents acid generation by inhibiting LDH enzyme at both the transcriptional and enzymatic levels. Furthermore it inhibits enolase, a key enzyme for glycolysis, resulting in decreased sugar internalization, glycolysis and acid production by streptococcus mutans cells[56].

Step 2- Effect on bacterial biofilm

In vitro, EGCG inhibited the formation and integrity of bacterial biofilms at concentrations between 156.25 to 625 μg/mL[56]. This was attributed to altered bacterial phenotype through catechin-mediated denaturation or deconformation of protein ligands, such as fimbriae. This subsequently hampered the proliferation and adherence of Streptococci to the tooth surface57. EGCG at MIC between 50 and 500 μg/mL inhibited S. mutans, and was bactericidal at a concentration of 1 mg/ml[55,58,59].

Step 3- Effect on F1Fo-ATPase and the agmatine deiminase systems

The F1Fo-ATPase and the agmatine deiminase systems are responsible for the aciduric nature of S. mutans[56,60]. They help in maintaining an optimal pH across the cell membrane, enabling the glycolysis at low pH within the biofilm[56].

EGCG suppresses both F1Fo-ATPase and agmatine deiminase systems, leading to energy deficit and disruption of ideal pH across the cell membrane[56]. Subsequently, the glucosyl transferase fails, resulting in decreased production of extra- and intracellular polysaccharides. This disrupts the biofilm integrity and adherence of bacteria to the tooth surface along with increased starvation stress.

Increased cytoplasmic acidity with inhibition of enolase and glycolysis diminishes the ATP pool, further impeding the activity of F1Fo-ATPase[56]. The impairment of LDH decreases the redox potential of the cell, leading to accumulation of glycolytic intermediates toxic to S. mutans[61]. This hinders its ability to sustain environmental stresses and even cell death[56].

A study showed that administration of green tea in the form of a mouth rinse (2 mg/mL of EGCG in 10 mL) inhibited a fall in pH, killed cultured cells of S. mutans time dependently and inhibited LDH activity. Thus, green tea mouth rinses could efficiently reduce acid production in dental plaque and S. mutans[62].

Step 4- Effect of Oxidative stress

Besides, the direct role of S. mutans, systemic host immune reactions, including oxidative stress, play an important role in caries progression. After the acidic erosion of enamel, a secondary inflammatory reaction is induced in the dentin, which provokes the inflammatory cascade. The bacterial toxins and ROS stimulate release of MMP, which degrade collagen in the dentin.

A recent review on the systemic theory of dental caries hypothesized that high-sugar intake provoked oxidative stress in the body and tooth decay63. Normally, the dentinal fluid provides nutrition and anti-oxidants to the cells of the tooth. Its flow is controlled by the endocrine portion of the parotid gland, which receives signals from the hypothalamus. Increased sucrose intake upregulates the free radical levels in the hypothalamus and decreases the parotid hormone production. Anti-oxidant supplementation could thus minimize the effects of ROS on the hypothalamus, and replenish the hormone levels as well as the dentinal fluid flow. This enhances the self-

cleansing ability and levels of tissue inhibitors of MMP in dentine, thereby preventing its degradation.[63] This was supported in a recent investigation showing the inhibitory effects of EGCG on MMP, which was more effective than sodium fluoride on acid erosion[64].

ii. Rosacea/Acne-

Not only does the main polyphenol component of green tea, EGCG, have antioxidant, immunomodulatory, and photoprotective properties, it is also marked by antiangiogenic and anti-inflammatory effects. In patients with significant facial erythema and telangiectasia, EGCG cream applied twice daily resulted in decreased expression of VEGF and HIF-1α, presumably explaining the efficacy of GTPs in the treatment of rosacea[65]. In addition, green tea extracts and especially EGCG have also been increasingly considered an effective candidate for the treatment of acne. Mechanisms of action include IGF-I-differentiated inhibition of lipogenesis as well as inflammation. Prospective studies on acne patients using a skin lotion with 2 % green tea extract daily have demonstrated efficacy[66,67].

Mechanism of action-

We found that EGCG suppresses the inflammatory response induced by heat-inactivated P. acnes in SEB-1 sebocytes, a well-established in vitro model of inflammatory acne, through the inhibition of NF-kB and AP-1 pathways. Although the mechanism by which EGCG regulates NF-kB and AP-1 pathways remains elusive, we hypothesize that it acts upstream of IkB degradation, based on our results showing that EGCG decreases phosphorylation of IkB. It is noteworthy that inhibition of AMPK rescued the EGCG-induced suppression of NF-kB and AP-1 pathways, suggesting that EGCG-activated AMPK suppresses the activity of the NF-kB and AP-1 pathways. Consistent with these observations, an increasing body of evidence demonstrates that AMPK inhibits the NF-kB pathway as well as the inflammatory response in the different types of cells[68,69,70]. It is also remarkable that EGCG decreases IL-1a in HaCaT keratinocytes, based on the fact that IL-1a induces hypercornification of the infundibulum in a manner similar to that seen in comedones[71]. These results suggest that EGCG might reverse the altered keratinization of follicular keratinocytes through the regulation of IL-1a. Together, these data provide insight to the molecular basis of the therapeutic effects of EGCG on the inflammatory acne lesions in our clinical trial. As apoptosis and cell cycle arrest can lead to drastic decreases in sebaceous glands' size and lipid contents, we examined whether EGCG has an antiproliferative effect. Indeed, we found that EGCG increases the levels of apoptosis and cell cycle arrest. The molecular mechanisms by which EGCG induces apoptosis and cell cycle arrest remain elusive, yet it is plausible to assume that inhibition of either NF-kB or Akt, or both, by EGCG causes apoptosis and cell cycle arrest, based on the fact that the NF-kB and Akt pathways are well recognized as prosurvival signals[72,73]. In addition, it is possible that EGCG activated AMPK may induce apoptosis or cell cycle arrest, as described in recent studies[74,75]. Further studies are needed to address this question. Our findings suggest that EGCG may promote apoptosis and cell cycle arrest in sebocytes, contributing to decreased sebaceous glands, and therefore mitigated acne lesions, similar to isotretinoin. P. acnes, a Gram-positive anaerobic bacterium, is a commensal of human skin, and its overgrowth is closely implicated in the progression of inflammation in acne[76,77]. Until recently, various antibiotics have been used to control the overgrowth of P. acnes, yet increasing antibiotic resistance[78,79] and biofilm formation[80] lead to a poor outcome. An accumulating body of evidence suggests that EGCG shows

antimicrobial activity against a diverse range of microorganisms, including bacteria, viruses, and fungi[81-83]. Indeed, we found that EGCG significantly inhibits the growth of P. acnes. As a possible mechanism, sophisticated molecular interactions between triphenols of EGCG and a peptide structure of bacterial proteins, including peptidoglycan, was suggested, because neither amino acid, alone or in combination, showed any effect on the antibiotic effect of EGCG[83]. This antibiotic effect of EGCG may provide an advantage as a therapeutic strategy for the treatment of acne, especially considering increasing concerns about antibiotic-resistant bacteria.

iii. In Hair disorders or Hair treatment-

There is some evidence that green tea extracts may be beneficial in hair disorders. By selectively inhibiting 5-alpha reductase activity, they can prevent or treat androgenetic alopecia. In ex vivo studies, EGCG also promotes hair growth, rendering it a potential future treatment option. Another possible future indication for GTPs may be hirsutism, as there is some evidence of ornithin decarboxylase (ODC) and 5-alpha reductase inhibition[84,85].

Cosmetic preparations containing tea extracts are recommended for patients with androgenetic alopecia and hair loss, regardless of gender. The occurrence of androgenic alopecia is directly related to the conversion of testosterone into more active dihydrotestosterone (DHT), which is mainly responsible for baldness. Hair follicles are particularly sensitive to DHT, which shortens the anagen phase of the hair growth cycle. As a result, most of the hair passes into the telogen phase, which is characterized by follicle miniaturization and reduction of hair roots. The newly growing hair is weaker—thinner and shorter and after several cycles, they stop to growth and hair loss can be observed[86]. In several studies tea polyphenols, essential oils and caffeine present in tea plant leaves inhibit the activity of 5α-reductase, which results in a decreased DHT formation[87,88]. The former compounds were also found stimulate hair roots and extend the hair growth phase (anagen phase)[48]. Therefore, constituents of tea are important ingredients of hair and scalp care cosmetics, which are especially recommended to individuals having excessive greasy hair and dandruff[89,46,48].

Fischer and co-investigators performed an in vitro study, which have shown that external application of caffeine in a concentration of 0.001% and 0.005% led to a significant stimulation of human hair follicle growth. It was concluded that caffeine reduces smooth muscle tension near the hair follicle and therefore significantly increases delivery of nutrients through the microcirculation of the papillae of the hair[88].

Green tea polyphenols were proved to significantly improve hair loss in mice. A group of 30 mice were fed with 50% fraction of polyphenol extract from dehydrated green tea in their drinking water for six months, whereas the control group received regular drinking water. Both groups received the same diet. The study revealed significant improvement in hair growth (33% of animals) in comparison to control group90. One of the main catechins present in green tea extract—EGCG was proved to be strong 5α-reductase and aromatase inhibitor [91,92]. This fact may significantly explain the effectiveness of using green tea polyphenols to treat androgenic alopecia, which is mainly associated with increased activity of these both enzymes. Such a mechanism was proved by Kwon and co-workers who evaluated the efficacy of EGCG on human hair growth. The study revealed that EGCG stimulated hair growth in hair follicles ex vivo culture and the proliferation of cultured human dermal papilla cells. Moreover, it was shown that epigallocatechin-3-gallate promoted hair

growth in vivo dermal papillae of human scalps. It was concluded that EGCG stimulates hair growth through dual proliferative and anti-apoptotic effect[93].

Mechanism of action-

DHQG(dihydroquercetin glucoside) has been combined with EGCG2, to prevent interleukin 8 release in scalp, and zinc and glycine (zinc being a co-factor for cystine incorporation in hair[94], and glycine being one of the key amino acid of the hair shaft[95]). This mix has been called Redensyl.(we can use hair lotion daily for three months over a whole head)

iv. Improvement of skin condition-

Green tea based cosmetic formulations are also popular to reduce increased sebum production, which is a main feature of an oily face. Sebum is a mixture of lipids, mainly squalene and wax esters, which is produced by sebaceous glands, especially on the face and scalp. Sebum production is hormonally regulated, and its increased production causes serious skin disorders[96]. Topical application of green tea extract may be very beneficial in reducing excessive sebum production and two independent clinical studies proved its effectiveness.

Mechanism of action-

Meethama and co-workers in a randomized single-blind, placebo-controlled study proved anti-sebum efficacy of a facial tonners containing green tea. The developed cosmetics contained 2%, 4.5% and 7% of green tea extract with 100 mg% of polyphenols, whereas the base consisted of hydroxyethyl cellulose, glycerin and panthenol. The study involved twenty healthy Thai volunteers (sixteen female and four male) aged between 20 and 35 years old. All tested products were stable and caused no skin irritation, which was proved using patch tests. Performed clinical investigation revealed significant anti-greasy and anti-sebum activity of a green tea extract, which in both cases were positively correlated with the concentration of the extract. Moreover it was proved that the effectiveness of a 28 days treatment was significantly better than 14 days. It was stated that cosmetics containing green tea extract might effectively improve the condition of oily face[97].

In a single-blinded, placebo controlled monocentric study performed by Mahmood and co-workers, a group of twenty two non-smoker, healthy men was investigated towards the effectiveness of a lotus and green tea topical application on facial sebum production. Volunteers were divided into two groups—in a first group men used green tea (5%) topical on one cheek and placebo control on another (n = 11). The second group used a combination of green tea and lotus (2.5% each) on one cheek and placebo control on another (n = 11). Both groups were asked to apply their respective topicals at bedtime for 60 days. Sebum secretion was measured using sebumeter in both groups at baseline and after 15, 30, 45 and 60 days. The study revealed a significant reduction of sebum production in both groups after 60 days of treatment—in the group applying only green tea and the combination of green tea and lotus, the sebum production was reduced by 27% and 25%, respectively. The performed study revealed that cosmetic therapy using green tea extract alone as well as a combination of green tea and lotus extracts may be a very effective tool in the treatment of skin disorders associated with increased sebum production[98].

In another study performed by Mahmood and co-workers ten healthy men aged 24–40 years old used topically to their cheeks a cosmetic formulation containing 3% of green tea extract. The experiment was conducted for eight weeks and a sebumeter was used to evaluate the reduction in sebum production, which was then calculated to a percentage value. Obtained

results revealed significant decrease in sebum production during the eight weeks study. The strongest effect was observed after eight weeks of treatment (the reduction of 60%). However, already after the first week significant improvement was noted (10%)87. It should be strongly emphasized that both of the above mentioned studies had significant limitations.

Skincare Products Containing Green Tea Extracts-

Tea extracts are important components of many cosmetics, including creams, moisturizing lotions, tonics, shower gels, hair products as well as cosmetic facial masks. That frequent use of Camellia sinensis extracts is due to its multidirectional effect. From all types of tea extracts, those obtained from green tea are the most widely used. These are proposed not only for young and problematic skin types, as they inhibit excessive sebum production, but can also be used by people with sensitive and allergic skin[99,100].

Tea Extract	Cosmetic Product	Cosmetic's Effects (Manufacturer's Declaration)
Green tea	Peeling mask	- Improved skin regeneration based on the antioxidant, anti-inflammatory and toning properties of green tea
Green tea	Face mask	- Strong soothing, anti-inflammatory and regenerative properties - antioxidant activity - Protection against harmful environmental influences
Green tea	Face mask	- Eliminated excess sebum - Proper skin hydration
Green tea	Shampoo	- Hair care for normal and slightly damaged hair - Antioxidant properties - Soothing action towards sensitive scalp (slightly moisturized and refreshed)
Green tea (Fuji)	Shampoo	- Hair care for normal hair - Refreshed and purified hair and scalp
Green tea (Matcha)	Shampoo	- Reduction of dandruff and greasy hair - Clarified and toned scalp - Intensive shine
Green tea	Shampoo	- Antioxidant in hair care (protection of hair against free radicals) - Hydrated and moisturized scalp
Green tea	Hair conditioner	- Hair care for all hair types - Protection against moisture loss - Strong antioxidant and hair growth stimulant properties - Smooth and soft hair
Green tea	Hair conditioner	- Strengthens hair - Antioxidant properties towards hair
Green tea	Hand and Body Lotion	- Nourishing cream for feet, hands and body - Makes the skin smooth and hydrated
Green tea	Body lotion	- A fresh fragrance - Refreshing body and mind - Improved mood
Green tea	Balancing lotion	- Superior hydration and nourishment of the skin - Softened and smoothed, cleansed skin leaving
Green tea	Refreshing body lotion	- Hydrated skin - Skin fragrance for a long time
Green tea	Body cream	- Nourished and moisturized skin - Smoothed skin - Soft and flexible skin - Skin care for all skin types
Green tea (Fuji)	Hand cream	- Nourished hands' skin - Softer and smoother hands
Green tea (Matcha)	Hand cream	- Skin care for all skin types - Nourished and moisturized skin of the hands
Green tea	Eye cream	- Removed six types of wrinkles under the eyes - Improved production of hyaluronic acid by epidermal cells - Restored moisture in the skin to fill fine lines in dry skin

CONCLUSION-

Green tea is a potent functional food for older adults. Recent scientific evidence explaining the mechanism of action and its activities suggest its promising role in the management of periodontitis, dental caries, dentinal erosion, and halitosis. Clinical experimental conditions showed that formulations containing Green Tea extracts have significant skin moisturizing effects. They improve skin microrelief (skin texture). The improvement in skin conditions and enhancement in the performance of cosmetic products suggest that Green Tea extracts are promising botanical ingredients in cosmetic formulations. The years of safe consumption of this beverage, supported by the numerous studies showing health benefits, warrant a general recommendation to consume it regularly. Finally a food processing sector must try to process Green Tea in a way that can enhance shelf life and also retain its natural aroma and flavour.

References

1. https://www.google.com/search/biological-source-of-green-tea-family
2. https://www.encyclopedia.com/literature-and-arts/literature-other-modern-languages/russian-and-eastern-european-literature/green-tea
3. J Dylewska- Grzelakowska. Kosmetyka Stosowana. 9th ed. WSziP; Warsaw, Poland: 2010; 71–74.
4. H Fujiki, M Suganuma, M Kurusu, S Okabe, Y Imayoshi, S Taniguchi, T Yoshida. New TNF-α releasing inhibitors as cancer preventive agents from traditional herbal medicine and combination cancer prevention study with EGCG and sulindac or tamoxifen. Mutat. Res./Fund. Mol. M. 2003;523,119-125.
5. Butt MS, Sultan MT. Green tea: nature's defense against malignancies. Crit. Rev. Food Sci. Nutr. 2009;49(5),463-73.
6. Atsumi T, Tonosaki K, Fujisawa S. Salivary free radical-scavenging activity is affected by physical and mental activities. Oral diseases. 2008 Sep;14(6):490-6.
7. Tsuchiya H. Effects of green tea catechins on membrane fluidity. Pharmacology. 1999;59(1):34-44.
8. Fassina G, Buffa A, Benelli R, Varnier OE, Noonan DM, Albini A. Polyphenolic antioxidant (–)-epigallocatechin-3-gallate from green tea as a candidate anti-HIV agent. Aids. 2002 Apr 12;16(6):939-41.
9. Yamaguchi K, Honda M, Ikigai H, Hara Y, Shimamura T. Inhibitory effects of (−)-epigallocatechin gallate on the life cycle of human immunodeficiency virus type 1 (HIV-1). Antiviral research. 2002 Jan 1;53(1):19-34.
10. Kawai K, Tsuno NH, Kitayama J, Okaji Y, Yazawa K, Asakage M, Hori N, Watanabe T, Takahashi K, Nagawa H. Epigallocatechin gallate, the main component of tea polyphenol, binds to CD4 and interferes with gp120 binding. Journal of Allergy and Clinical Immunology. 2003 Nov 1;112(5):951-7.
11. Verma P, Mukherjee A, Shrivastava D, Gurjar H, Sonu K, A Review On:Green Tea:A Miraculous Drink, International Journal of Pharmaceutical Sciences Review and Research, 2018; 51(2):27
12. https://www.google.com/search=role+of+green+tea+in+cosmetics
13. Arct J, Pytkowska K. Flavonoids as components of biologically active cosmeceuticals. Clinics in dermatology. 2008 Jul 1;26(4):347-57.
14. Béliveau R, Gingras D. Green tea: prevention and treatment of cancer by nutraceuticals. The Lancet. 2004 Sep 18;364(9439):1021-2.

15. Graham HN. Green tea composition, consumption, and polyphenol chemistry. Preventive medicine. 1992 May 1;21(3):334-50.
16. Yamamoto T, Juneja LR, Kim M. Chemistry and applications of green tea. CRC press; 1997 Jul 31.
17. Manach C, Scalbert A, Morand C, Rémésy C, Jiménez L. Polyphenols: food sources and bioavailability. The American journal of clinical nutrition. 2004 May 1;79(5):727-47.
18. Stevenson DE, Hurst RD. Polyphenolic phytochemicals–just antioxidants or much more?. Cellular and Molecular Life Sciences. 2007 Nov;64(22):2900-16.
19. Heinrich U, Neukam K, Tronnier H, Sies H, Stahl W. Long-term ingestion of high flavanol cocoa provides photoprotection against UV-induced erythema and improves skin condition in women. The Journal of nutrition. 2006 Jun 1;136(6):1565-9.
20. Neukam K, Stahl W, Tronnier H, Sies H, Heinrich U. Consumption of flavanol-rich cocoa acutely increases microcirculation in human skin. European journal of nutrition. 2007 Feb 1;46(1):53-6.
21. Sun CL, Yuan JM, Koh WP, Yu MC. Green tea, black tea and breast cancer risk: a meta-analysis of epidemiological studies. Carcinogenesis. 2006 Jul 1;27(7):1310-5.
22. Verma P, Mukherjee A, Shrivastava D, Gurjar H, Sonu K, A Review On:Green Tea:A Miraculous Drink, International Journal of Pharmaceutical Sciences Review and Research, 2018; 51(2):27
23. Evensen NA, Braun PC. The effects of tea polyphenols on Candida albicans: inhibition of biofilm formation and proteasome inactivation. Canadian journal of microbiology. 2009 Sep;55(9):1033-9.
24. Nakanishi T, Mukai K, Yumoto H, Hirao K, Hosokawa Y, Matsuo T. Anti-inflammatory effect of catechin on cultured human dental pulp cells affected by bacteria-derived factors. European journal of oral sciences. 2010 Apr;118(2):145-50.
25. Klass CM, Shin DM. Current status and future perspectives of chemoprevention in head and neck cancer. Current cancer drug targets. 2007 Nov 1;7(7):623-32.
26. Byun EB, Choi HG, Sung NY, Byun EH. Green tea polyphenol epigallocatechin-3-gallate inhibits TLR4 signaling through the 67-kDa laminin receptor on lipopolysaccharide-stimulated dendritic cells. Biochemical and biophysical research communications. 2012 Oct 5;426(4):480-5.
27. Katiyar SK, Agarwal R, Mukhtar H. Protection against malignant conversion of chemically induced benign skin papillomas to squamous cell carcinomas in SENCAR mice by a polyphenolic fraction isolated from green tea. Cancer research. 1993 Nov 15;53(22):5409-12.
28. Zink A, Traidl-Hoffmann C. Green tea in dermatology–myths and facts. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2015 Aug;13(8):768-75.
29. Frezza M, Schmitt S, Ping Dou Q. Targeting the ubiquitin-proteasome pathway: an emerging concept in cancer therapy. Current topics in medicinal chemistry. 2011 Dec 1;11(23):2888-905.
30. Cohen S, Carpenter G, King Jr L. Epidermal growth factor-receptor-protein kinase interactions. Co-purification of receptor and epidermal growth factor-enhanced phosphorylation activity. Journal of Biological Chemistry. 1980 May 25;255(10):4834-42.
31. Wieduwilt MJ, Moasser M. The epidermal growth factor receptor

family: biology driving targeted therapeutics. Cellular and Molecular Life Sciences. 2008 May;65(10):1566-84.
32. Masuda M, Suzui M, Weinstein IB. Effects of epigallocatechin-3-gallate on growth, epidermal growth factor receptor signaling pathways, gene expression, and chemosensitivity in human head and neck squamous cell carcinoma cell lines. Clinical cancer research. 2001 Dec 1;7(12):4220-9.
33. He Z, Tang F, Ermakova S, Li M, Zhao Q, Cho YY, Ma WY, Choi HS, Bode AM, Yang CS, Dong Z. Fyn is a novel target of (−)-epigallocatechin gallate in the inhibition of JB6 Cl41 cell transformation. Molecular Carcinogenesis: Published in cooperation with the University of Texas MD Anderson Cancer Center. 2008 Mar;47(3):172-83.
34. Woodworth CD, Gaiotti D, Michael E, Hansen L, Nees M. Targeted disruption of the epidermal growth factor receptor inhibits development of papillomas and carcinomas from human papillomavirus-immortalized keratinocytes. Cancer research. 2000 Aug 15;60(16):4397-402.
35. Takai S, Matsushima-Nishiwaki R, Adachi S, Natsume H, Minamitani C, Mizutani J, Otsuka T, Tokuda H, Kozawa O. (-)-Epigallocatechin gallate reduces platelet-derived growth factor-BB-stimulated interleukin-6 synthesis in osteoblasts: suppression of SAPK/JNK. Mediators of inflammation. 2008 Oct;2008.
36. Sukhthankar M, Yamaguchi K, Lee SH, McEntee MF, Eling TE, Hara Y, Baek SJ. A green tea component suppresses posttranslational expression of basic fibroblast growth factor in colorectal cancer. Gastroenterology. 2008 Jun 1;134(7):1972-80.
37. Im M, Kim SY, Sohn KC, Choi DK, Lee Y, Seo YJ, Kim CD, Hwang YL, Zouboulis CC, Lee JH. Epigallocatechin-3-gallate suppresses IGF-I-induced lipogenesis and cytokine expression in SZ95 sebocytes. Journal of investigative dermatology. 2012 Dec 1;132(12):2700-8.
38. Noda T, Ojima T, Hayasaka S, Murata C, Hagihara A. Gargling for oral hygiene and the development of fever in childhood: a population study in Japan. Journal of epidemiology. 2012 Jan 5:1111210269-.
39. https://www.google.com/search=green+tea+efect+in+gargling
40. Verma P, Mukherjee A, Shrivastava D, Gurjar H, Sonu K, A Review On:Green Tea:A Miraculous Drink, International Journal of Pharmaceutical Sciences Review and Research, 2018; 51(2):30
41. https://www.google.com/search?q=beneficial+effect+of+green+tea+in+gargling
42. Page RC, Kornman KS. The pathogenesis of human periodontitis: an introduction. Periodontology 2000. 1997 Jun;14(1):9-11.
43. Priya BM, Anitha V, Shanmugam M, Ashwath B, Sylva SD, Vigneshwari SK. Efficacy of chlorhexidine and green tea mouthwashes in the management of dental plaque-induced gingivitis: A comparative clinical study. Contemporary clinical dentistry. 2015 Oct;6(4):505.
44. Jayakeerthana S. Benefits of Green Tea: A Revie. Journal of Pharmaceutical Sciences and Research. 2016 Oct 1;8(10):1184.
45. Rawlings AV. Cellulite and its treatment. International journal of cosmetic science. 2006 Jun;28(3):175-90.
46. Koch W, Zagórska J, Marzec Z, Kukula-Koch W. Applications of tea (Camellia sinensis) and its active constituents in cosmetics. Molecules. 2019 Jan;24(23):4277.
47. 47. Romer, M. Aromaterapia. Leksykon Roślin Leczniczych

(Aromatherapy. Lexicon of Medicinal Plants), 1 st ed.; MedPharm: Polska, Wrocław, Poland, 2007; pp. 39–41.
48. Majewska K, Olender D, Pawełczyk A, Zaprutko T, Żwawiak J, Zaprutko L. Aktywne kosmetyki wśród produktów spożywczych. Homines Hominibus. 2010;6:65-96.
49. Rao J, Paabo KE, Goldman MP. A double-blinded randomized trial testing the tolerability and efficacy of a novel topical agent with and without occlusion for the treatment of cellulite: a study and review of the literature. Journal of drugs in dermatology: JDD. 2004 Jul 1;3(4):417-25.
50. Chen N, Bezzina R, Hinch E, Lewandowski PA, Cameron-Smith D, Mathai ML, Jois M, Sinclair AJ, Begg DP, Wark JD, Weisinger HS. Green tea, black tea, and epigallocatechin modify body composition, improve glucose tolerance, and differentially alter metabolic gene expression in rats fed a high-fat diet. Nutrition research. 2009 Nov 1;29(11):784-93.
51. Wang S, Moustaid-Moussa N, Chen L, Mo H, Shastri A, Su R, Bapat P, Kwun I, Shen CL. Novel insights of dietary polyphenols and obesity. The Journal of nutritional biochemistry. 2014 Jan 1;25(1):1-8.
52. https://teaperspective.com/make-your-own-green-tea-moisturizer/
53. https://www.femina.in/beauty/skin/the-skin-benefits-of-green-tea-109426.html
54. Niakan M, Naderi NJ, Fard MJ. Antibacterial Activity of Iranian Green and Black Tea on Streptococcus Mutans: An In Vitro Study. Journal of Dentistry of Tehran University of Medical Sciences-It, s Title Changed. 2011 Jul 23;8(2).
55. Taylor PW, Hamilton-Miller JM, Stapleton PD. Antimicrobial properties of green tea catechins. Food science and technology bulletin. 2005;2:71.
56. Xu X, Zhou XD, Wu CD. The tea catechin epigallocatechin gallate suppresses cariogenic virulence factors of Streptococcus mutans. Antimicrobial agents and chemotherapy. 2011 Mar;55(3):1229.
57. Beretta G, Furlanetto S, Regazzoni L, Zarrella M, Facino RM. Quenching of α, β-unsaturated aldehydes by green tea polyphenols: HPLC–ESI–MS/MS studies. Journal of Pharmaceutical and Biomedical Analysis. 2008 Nov 4;48(3):606-11.
58. Sakanaka S, Aizawa M, Kim M, Yamamoto T. Inhibitory effects of green tea polyphenols on growth and cellular adherence of an oral bacterium, Porphyromonas gingivalis. Bioscience, biotechnology, and biochemistry. 1996 Jan 1;60(5):745-9.
59. Kawamura J, Takeo T. Antibacterial activity of tea catechin to Streptococcus mutans. Nippon Shokuhin Kogyo Gakkaishi. 1989 Jun 15;36(6):463-7.
60. Lemos JA, Burne RA. A model of efficiency: stress tolerance by Streptococcus mutans. Microbiology (Reading, England). 2008 Nov;154(Pt 11):3247.
61. Ahmed S, Wang N, Lalonde M, Goldberg VM, Haqqi TM. Green tea polyphenol epigallocatechin-3-gallate (EGCG) differentially inhibits interleukin-1β-induced expression of matrix metalloproteinase-1 and-13 in human chondrocytes. Journal of Pharmacology and Experimental Therapeutics. 2004 Feb 1;308(2):767-73.
62. Hirasawa M, Takada K, Otake S. Inhibition of acid production in dental plaque bacteria by green tea catechins. Caries research. 2006;40(3):265-70.
63. Southward K. The systemic theory of dental caries. General dentistry. 2011 Sep 1;59(5):367-73.
64. Kato MT, Leite AL, Hannas AR, Buzalaf MA. Gels containing MMP

inhibitors prevent dental erosion in situ. Journal of dental research. 2010 May;89(5):468-72.
65. Santo Domingo D, Camouse MM, Hsia AH, Matsui M, Maes D, Ward NL, Cooper KD, Baron ED. Anti-angiogenic effects of epigallocatechin-3-gallate in human skin. International journal of clinical and experimental pathology. 2010;3(7):705.
66. Reuter J, Wölfle U, Weckesser S, Schempp C. Which plant for which skin disease? Part 1: Atopic dermatitis, psoriasis, acne, condyloma and herpes simplex. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2010 Oct;8(10):788-96.
67. Elsaie ML, Abdelhamid MF, Elsaaiee LT, Emam HM. The efficacy of topical 2% green tea lotion in mild-to-moderate acne vulgaris. Journal of drugs in dermatology: JDD. 2009 Apr 1;8(4):358-64.
68. Navarro-Peran E, Cabezas-Herrera J, Sanchez-Del-Campo L, Garcia-Canovas F, Rodríguez-López JN. The anti-inflammatory and anti-cancer properties of epigallocatechin-3-gallate are mediated by folate cycle disruption, adenosine release and NF-κB suppression. Inflammation Research. 2008 Oct;57(10):472-8.
69. Green CJ, Macrae K, Fogarty S, Hardie DG, Sakamoto K, Hundal HS. Counter-modulation of fatty acid-induced pro-inflammatory nuclear factor κB signalling in rat skeletal muscle cells by AMP-activated protein kinase. Biochemical Journal. 2011 Apr 15;435(2):463-74.
70. Morizane Y, Thanos A, Takeuchi K, Murakami Y, Kayama M, Trichonas G, Miller J, Foretz M, Viollet B, Vavvas DG. AMP-activated protein kinase suppresses matrix metalloproteinase-9 expression in mouse embryonic fibroblasts. Journal of Biological Chemistry. 2011 May 6;286(18):16030-8.
71. Guy R, Green MR, Kealey T (1996) Modeling acne in vitro. J Invest Dermatol 106:176–82
72. Beg AA, Baltimore D. An essential role for NF-κB in preventing TNF-α-induced cell death. Science. 1996 Nov 1;274(5288):782-4.
73. Chen W, Borchers AH, Dong Z, Powell MB, Bowden GT. UVB irradiation-induced activator protein-1 activation correlates with increased c-fos gene expression in a human keratinocyte cell line. Journal of Biological Chemistry. 1998 Nov 27;273(48):32176-81.
74. Motoshima H, Goldstein BJ, Igata M, Araki E. AMPK and cell proliferation–AMPK as a therapeutic target for atherosclerosis and cancer. The Journal of physiology. 2006 Jul 1;574(1):63-71.
75. Hwang JT, Ha J, Park IJ, Lee SK, Baik HW, Kim YM, Park OJ. Apoptotic effect of EGCG in HT-29 colon cancer cells via AMPK signal pathway. Cancer letters. 2007 Mar 8;247(1):115-21.
76. Kim J. Review of the innate immune response in acne vulgaris: activation of Toll-like receptor 2 in acne triggers inflammatory cytokine responses. Dermatology. 2005;211(3):193-8.
77. Michalak-Stoma A, Tabarkiewicz J, Olender A, Juszkiewicz-Borowiec M, Stoma F, Pietrzak A, Pozarowski P, Bartkowiak-Emeryk M. The effect of Propionibacterium acnes on maturation of dendritic cells derived from acne patients' peripherial blood mononuclear cells. Folia histochemica et cytobiologica. 2008;46(4):535-9.
78. Strauss JS, Krowchuk DP, Leyden JJ, Lucky AW, Shalita AR, Siegfried EC, Thiboutot DM, Van Voorhees AS, Beutner KA, Sieck CK, Bhushan R. Guidelines of care for acne vulgaris management. Journal of the American Academy of Dermatology. 2007 Apr 1;56(4):651-63.

79. Thiboutot DM. Overview of acne and its treatment. Cutis. 2008 Jan 1;81(1 Suppl):3-7.
80. Burkhart CG, Burkhart CN. Expanding the microcomedone theory and acne therapeutics: Propionibacterium acnes biofilm produces biological glue that holds corneocytes together to form plug.
81. Alexis AF, Jones VA, Stiller MJ. Potential therapeutic applications of tea in dermatology. International journal of dermatology. 1999 Oct;38(10):735-43.
82. Dufresne CJ, Farnworth ER. A review of latest research findings on the health promotion properties of tea. The Journal of nutritional biochemistry. 2001 Jul 1;12(7):404-21.
83. Yoda Y, Hu ZQ, Shimamura T, Zhao WH. Different susceptibilities of Staphylococcus and Gram-negative rods to epigallocatechin gallate. Journal of Infection and Chemotherapy. 2004 Jan 1;10(1):55-8.
84. Reuter J, Wölfle U, Korting HC, Schempp C. Which plant for which skin disease? Part 2: Dermatophytes, chronic venous insufficiency, photoprotection, actinic keratoses, vitiligo, hair loss, cosmetic indications. JDDG: Journal der Deutschen Dermatologischen Gesellschaft. 2010 Nov;8(11):866-73.
85. Namazi MR, Feily A. Green tea extract: a novel addition to the antihirsutism armamentarium?. The Journal of Alternative and Complementary Medicine. 2009 Jul 1;15(7):700-1.
86. Mnich CD, Hoek KS, Virkki LV, Farkas A, Dudli C, Laine E, Urosevic M, Dummer R. Green tea extract reduces induction of p53 and apoptosis in UVB-irradiated human skin independent of transcriptional controls. Experimental dermatology. 2009 Jan;18(1):69-77.
87. Mahmood T, Akhtar N, Moldovan C. A comparison of the effects of topical green tea and lotus on facial sebum control in healthy humans. Hippokratia. 2013 Jan;17(1):64.
88. Fischer TW, Hipler UC, Elsner P. Effect of caffeine and testosterone on the proliferation of human hair follicles in vitro. International journal of dermatology. 2007 Jan;46(1):27-35.
89. Lamer-Zarawska E, Kowal-Gierczak B, Niedworok J, editors. Fitoterapia i leki roślinne. Wydawnictwo Lekarskie PZWL; 2007.
90. Esfandiari A, Kelly AP. The effects of tea polyphenolic compounds on hair loss among rodents. Journal of the National Medical Association. 2005 Aug;97(8):1165.
91. Hiipakka RA, Zhang HZ, Dai W, Dai Q, Liao S. Structure–activity relationships for inhibition of human 5α-reductases by polyphenols. Biochemical pharmacology. 2002 Mar 15;63(6):1165-76.
92. Satoh K, Sakamoto Y, Ogata A, Nagai F, Mikuriya H, Numazawa M, Yamada K, Aoki N. Inhibition of aromatase activity by green tea extract catechins and their endocrinological effects of oral administration in rats. Food and Chemical Toxicology. 2002 Jul 1;40(7):925-33.
93. Kwon O.S., Han J.H., Yoo H.G., Chung J.H., Cho K.H., Eun H.C., Kim K.H. Human hair growth enhancement in vitro by green tea epigallocatechin-3-gallate (EGCG) Phytomed. 2007;14:551–555. doi: 10.1016/j.phymed.2006.09.009.
94. Hsu JM, Anthony WL. Impairment of cystine-35S incorporation into skin protein by zinc-deficient rats. The Journal of nutrition. 1971 Apr 1;101(4):445-52.
95. Rogers GE. Hair follicle differentiation and regulation. International Journal of

Developmental Biology. 2003 Jan 1;48(2-3):163-70.
96. Saric S, Notay M, Sivamani RK. Green tea and other tea polyphenols: Effects on sebum production and acne vulgaris. Antioxidants. 2017 Mar;6(1):2.
97. Meetham P, Kanlayavattanakul M, Lourith N. Development and clinical efficacy evaluation of anti-greasy green tea tonner on facial skin. Revista Brasileira de Farmacognosia. 2018 Apr;28(2):214-7.
98. Mahmood T, Akhtar N, Khan BA, Khan HM, Saeed T. Outcomes of 3% green tea emulsion on skin sebum production in male volunteers. Bosnian journal of basic medical sciences. 2010 Aug;10(3):260.
99. Lamer-Zarawska E, Kowal-Gierczak B, Niedworok J, editors. Fitoterapia i leki roślinne. Wydawnictwo Lekarskie PZWL; 2007.
100. Gabor M. Pharmacologic effects of flavonoids on blood vessels. Journal of Vascular Research. 1972;9(3-6):355-74.