(Review Article)

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Green Tea Polyphenols: Versatile Cosmetic Ingredient

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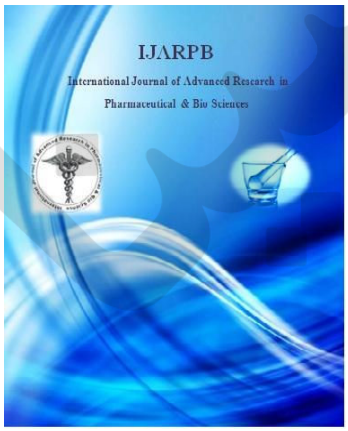

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ABSTRACT

The research and development of cosmeceuticals is booming in recent years. Many substances, from botanical are tested or investigated as the active ingredients in cosmeceuticals. Green tea polyphenols have gained high popularity in cosmetic arena for their skin improving property. This review is an attempt to collect the scientific data of green tea polyphenols on major cosmetic problems like aging, wrinkle, photo-damage, skin darkness, acne, dandruff and hair loss. This communication covers green tea effect, their mechanism of action and clinical trials conducted on humans for different cosmetological conditions.

KEY WORD: GTC, EGC, ECG, EGCG, Green tea, Photoprotection, Antidandruff

(Review Article)

INTRODUCTION

Increasing spending power has made the cosmetic industry one of the rapidly growing sectors in India. Indian cosmetic sector analysis (2009-2012) done by market researchers RNCOS shows that the last year sale of cosmetics in India was around INR 356.6bn. Herbs have been used in medicines and cosmetics from centuries. Their potential to treat different skin diseases, to adorn and improve the skin appearance is well-known. The tea plant, *Camellia sinensis*, is a member of the Theaceae family. Tea is a large shrub with white flowers and is indigenous to Asia and China, but commercially grown in Africa, Sri Lanka, Malaysia and Indonesia. The young leaves and buds are used for production of black, oolong, and green tea. Unlike black and oolong tea, green tea production does not involve oxidation of young tea leaves. Green tea is produced from steaming fresh leaves at high temperatures, thereby inactivating the oxidizing enzymes and leaving the polyphenol content intact. Various extraction methods have been reported in the literature like microwave extraction, ultrasonic extraction, Soxhlet extraction, heat reflux extraction and ultrahigh pressure extraction for extraction of polyphenols from green tea. Caffeine may be excluded in green tea extracts in order to avoid side effects ; caffeine free green tea extract supplements are now available.[1]

The cardinal antioxidative ingredient in the green tea extract is green tea catechins (GTC), which comprise four major epicatechins derivative; namely, epicatechin(EC),epigallocatechin(EGC), epicatechin gallate (ECG), and epigallocatechin gallate (EGCG). Other components include three kinds of flavonoids, known as kaempferol, quercetin, and myricetin.[2] A remarkably higher content of myricetin is detected in tea and its extracts than in many other plants, and this high concentration of myricetin may have some implications with the bioactivity of tea and its extracts.[3]

CHEMICAL PROPERTIES

Green tea extract is 20 times more antioxidant-active than Vitamin C. The main attribution is supposed to be EGCG.[4] In alkaline solutions (pH > 8) GTC (green tea catechins) is rather unstable; in acidic solutions (pH < 4), however, GTC shows excellent stability. The stability in alkaline solutions varies between four components of GTC in green tea extracts. Recent study demonstrates that EGCG and EGC is more unstable than EC and ECG in a basic solution, giving an explanation to the fact that EGCG and EGC do not circulate in the basic sodium phosphate buffer fluid of human body.[5] In a high temperature environment, GTC is not stable: an epimerization change is likely to occur, because heating results in the conversion from EGCG to GCG.[5] Thus it is considered inappropriate to infuse green tea or its extracts with overheated water.

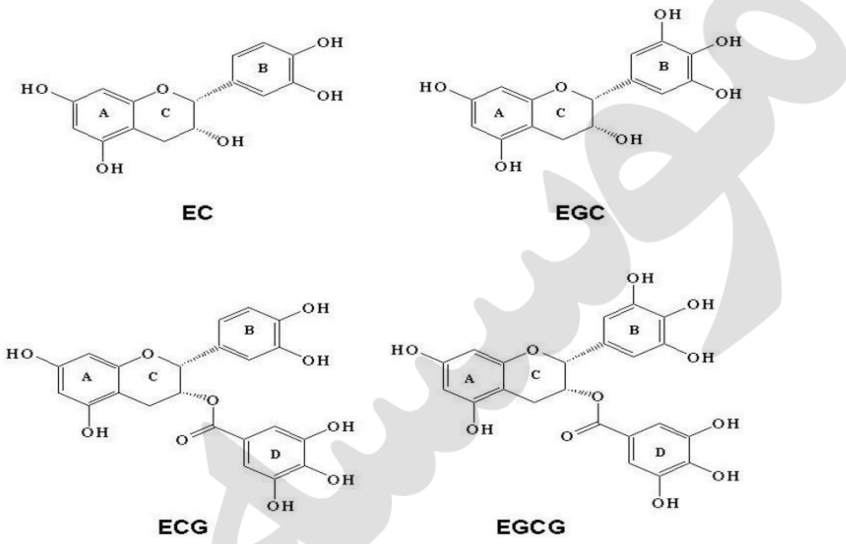

Figure 1: Major constituents of green tea

BIOCHEMICAL PROPERTIES

The biochemical properties of green tea extracts can be generally divided into four aspects – antioxidant, anticarcinogen, anti-inflammatory, and anti-radiation.[3,6] Green tea extracts exhibit stronger antioxidant protection for human body than vitamin C and vitamin E.[7] Scavenging effect of lipid free-radicals (one antioxidant property) of polyphenols in green tea extracts can be clearly observed in experiments.[6] The ability of GTP in green tea extracts to eliminate lipid-derived free radicals is noticeably stronger (almost 50 times) than that of ginkgo biloba extracts.[6] Further investigations indicate that the boosting level of superoxide dismutase (SOD) and glutathione dismutase (GSHPx) may account for the inhibitory effect of GTC against lipid oxidation (rancidification).[5] Moreover, the anticarcinogenic property make the green tea extracts a hotspot in recent scientific researches.

In many experiments, green tea extracts show inhibitory effects on cancer cells. In vitro assays, Catechin and caffeine, which are main components in green tea extracts, block the cell cycle of cancer cells (cytotoxicity) and induce programmed cell death[3]; in vivo, green tea extracts also inhibits prostatic carcinoma transplanted in nude mice.[6]

In addition, green tea extracts also contain a wide-ranged anti-inflammatory characteristic, so it may be helpful in treating chronic inflammatory states.[3] The bactericidal activity against S.mutans is conspicuous in Japanese green tea extracts[6], and the maltose level in mouth is consistently lower after drinking tea.[3] Therefore, green tea extracts may be effective in oral hygiene maintenance. Green tea extracts show anti-radiation properties on white rats in radioactive isotope experiments.[6]

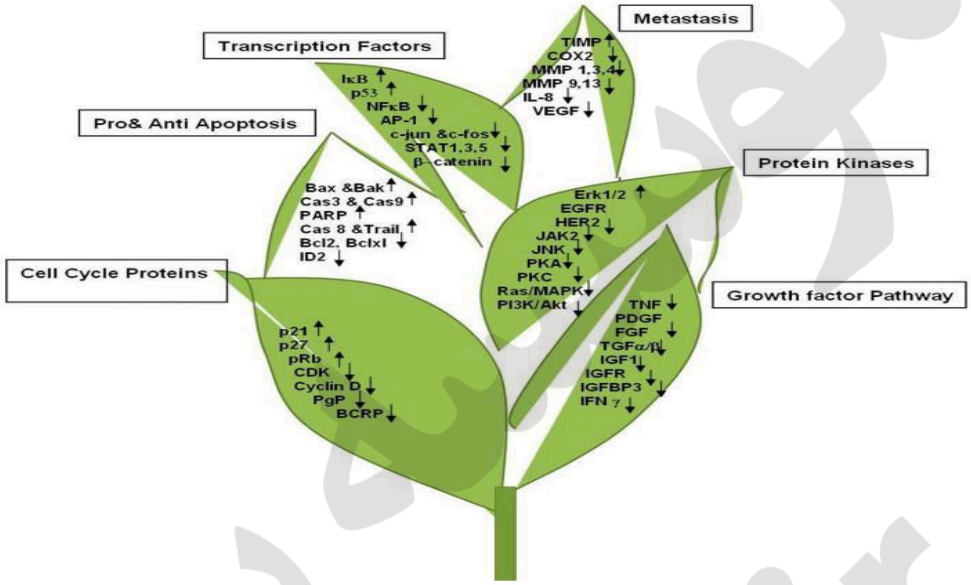

Figure 2: Green tea leaf chemical mediators

Table 1: Medicinal uses of GTP

Application	Mechanism	Reference
Antibacterial	Inhibition of β-lactamases, reverse transcriptase of HIV, collagenase, fatty acid synthtase and various other enzymes.	8
Anticancer	Inhibition of mitogen-activated protein kinases (MAPK), growth factor related cell signaling, activation of activator protein 1 (AP-1) and nuclear factor-B (NF-kappaB), topoisomerase I, matrix metalloproteinases and other potential targets.	9
Anti inflammatory	Inhibition inflammasome down regulation→decreased IL-1β secretion→decreased NF-κB activities→decreased cell growth.	10
Anti radiation	Reduces the ROS generation and apoptosis.	11
Anti obesity	Inhibition of the enzymes catechol-O methyl transferase, acetyl-CoA carboxylase, fatty acid synthase and impeding absorption of fat via the gut.	12
Antiacne	Decreased sebum production Antimicrobial effect on Acne vulgaris.	13

Nonalcoholic fatty liver disease	Through decrease dietary lipid absorption, hypolipidemic ,antioxidant and anti-inflammatory.	14
Diabetes	Increased expression level of glucose transporter IV.	15.
Atherosclerosis	Reduce LDL oxidizability, Improves vascular function.	16,17
Dental cavities	Reduces VSCs by suppressing mgl, the gene encoding L-methionine-α-deamino-γ mercaptomethanelyase.	18
Intestinal dysbiosis	Rise levels of Lactobacilli and Bifidobacteria while lowering levels of Enterobacteriaceae, Bacteroidaceae, and eubacteria.	19
Pneumonia	Inhibit endotoxin-induced HMGB1 release.	20
Diarrhea	Inhibitory effect on Helicobacter pylori infection.	21
Pyelonephritis	Inhibit carcinogen-induced increases in the oxidized DNA base, 8-hydroxy-2'-deoxyguanosine.	22
Cystitis	Protect against oxidative stress/damage and bladder cell death.	23
Antiviral	Inhibits virus infection and maturation cleavages carried out by adenin.	24
Neuroprotective	Implicated in brain senescence.	25
Antiangiogenic	Inhibition of VEGF transcription.(vascular endothelial growth factor).	26
Antioxidative	Inhibited oxygen consumption and formation of conjugated dienes in AAPH-mediated linoleic acid peroxidative reaction.	27
Atherosclerotic markers	Decrease the levels of ox-LDL and soluble vascular cell adhesion molecule-1 (sVCAM-1).	28

GREEN TEA CATECHINS IN COSMETOLOGY

AGING AND ANTIWRINKLE

Free radicals are known to promote oxidation of nucleic acids, proteins, and lipids and can damage intracellular structures including DNA.[29] Free radicals also up-regulate transcription factors, such as activator protein 1 (AP-1) and nuclear transcription factor-kappa B (NF-kB). AP-1 is responsible for production of metalloproteinases that breakdown existing collagen, contributing to skin wrinkling.[30] NF-kB up-regulates transcription of proinflammatory mediators, such as interleukin (IL)-1, IL-6, IL-8, and tumor necrosis factor-alpha.[31] Acting through the cell surface, these proinflammatory mediators further activate AP-1 and NF-kB, resulting in more damage. It is the sum of these events that are responsible for skin aging.[32] Green tea and EGCG in addition to being effective free-radical scavengers, down-regulate UV-induced expression of AP-1 and NF-kB and suppress metalloproteinase and age-related collagen cross-linking in mice. In addition,

it has been shown *in vitro* that green tea polyphenols inhibit the activity of collagenase and increases collagen biosynthesis rate of human fibroblasts.[33] Diana Santo Domingo et al conducted a small randomized, double blind, split face trial using a cream containing 2.5% w/w of EGCG. Four healthy volunteers with significant erythema and telangiectasia on the face applied EGCG cream to one side of the face, and vehicle control cream to the other, twice daily for six weeks. After six weeks, biopsies were taken from EGCG and vehicle treated sites. Immuno histochemistry was used to measure VEGF and HIF-1α. HIF-1α expression was decreased in EGCG treated sites, such that 28.4% of the epidermis showed positive staining in vehicle treated vs. 13.8% in EGCG treated sites ($p<0.001$). A similar decrease in VEGF expression was found (6.7% in EGCG vs. 11.0%in in vehicle-treated skin ($p<0.005$). EGCG topical treatments influence HIF-1α induction and VEGF expression and may serve as a potential agent in the prevention of telangiectasias.[34]

PHOTOPROTECTION

Dietary constituents including polyphenols contribute to endogenous photoprotection and modulate skin characteristics related to structure and function of the tissue.

In a study conducted by Tubesing K et al, human skin was pretreated with either green tea extract or one of its constituents and then exposed to two minimal erythema doses of solar stimulated light. Application of green tea extract and/or one of its constituents resulted in dose dependent inhibition of UV-induced erythema. EGCG and ECG were the most efficient components in suppressing UV-induced erythema when tested individually. It was also shown that green tea extract can reduce the DNA damage that occurs after UV radiation through inhibition of UV-induced erythema likely due to its antioxidant and anti-inflammatory effects.[35] Thus, it appears that topical application of green tea extract and some of its components may be useful for mitigating the adverse effects of sunlight on human skin, such as photoaging. In another study, topical green tea was shown to provide photoprotection anywhere from 24 hours up to 72 hours. It reduced the number of sunburned cells by 66 percent when applied 30 minutes prior to UVB exposure and when applied at 1- to 10- percent

concentrations. A dose dependent inhibition of ultra-violet induced erythema was evident.[36]

Heinrich U et.al in a 12-wk, double-blind, placebo-controlled study, 60 female volunteers were randomized to an intervention or control group. Participants consumed either a beverage with green tea polyphenols providing 1402 mg total catechins/d or a control beverage. Skin photoprotection, structure, and function were measured at baseline (wk 0), wk 6, and wk 12. Following exposure of the skin areas to 1.25 minimal erythemal dose of radiation from a solar simulator, UV-induced erythema decreased significantly in the intervention group by 16 and 25% after 6 and 12 wk, respectively. Skin structural characteristics that were positively affected included elasticity, roughness, scaling, density, and water homeostasis. Intake of the green tea polyphenol beverage for 12 wk increased blood flow and oxygen delivery to the skin. Likewise, in a separate, randomized, double-blind, single-dose (0.5, 1.0, and 2.0 g) study of green tea polyphenols, blood flow was maximized at 30 min after ingestion.

In summary, green tea polyphenols delivered in a beverage were shown to protect skin against harmful UV radiation and helped to improve overall skin quality of women.[37]

ANTI ACNE

Acne vulgaris is the most common skin condition observed in the medical community. Although we know that hormones are important in the development of acne, many questions remain unanswered regarding the mechanisms by which hormones exert their effects. Androgens such as dihydrotestosterone (DHT) and testosterone, the adrenal precursor dehydroepiandrosterone sulfate (DHEAS), estrogens such as estradiol, and other hormones, including growth hormone and insulin-like growth factors (IGFs), may be important in acne. It is not known whether these hormones are taken up from the serum by the sebaceous gland, whether they are produced locally within the gland, or whether a combination of these processes is involved. Finally, the cellular and molecular mechanisms by which these hormones exert their influence on the sebaceous gland have not been fully elucidated. Hormonal therapy is an option in women with acne not responding to conventional treatment or with signs of endocrine abnormalities.[38]

Mahmood T et al study depict potential effects of stable formulation (water in oil emulsion), containing 3% green tea (Camellia sinensis L) extract on skin sebum production in healthy human volunteers. Formulation was applied to the cheeks of healthy human volunteers (n=10) for a period of 8 weeks. Measurements for skin sebum production were considered using Sebumeter MPA 5. Results were compiled and any effect produced by the formulation was justified statistically. It was observable that statistically significant ($p < 0.5\%$) results were found for skin sebum production after long term application of the formulation.[39] In another study Elsaie ML et.al study green tea was given and applied twice daily for a period of 6 weeks. The patients were seen every 2 weeks to evaluate the lesions and any side effects. To determine efficacy on acne severity, the authors used both total lesion count (TLC) and their devised severity index (SI). Total lesions count (TLC) was calculated as papules + pustules while SI was scaled with numbers (1, 2 or 3) correlating to

TLC in order of increasing intensity. TLC < 10 was given an SI of 1, TLC 10-20 was given an SI of 2 and TLC > 20 was given an SI of 3. The mean total lesion count (TLC) decreased from 24 before the treatment to 10 after 6 weeks after treatment, a reduction of 58.33%. The difference was statistically significant (P < 0.0001, 95% confidence interval [CI] of the difference = 8.58 - 19.42). The mean severity index (SI) decreased from 2.05 before treatment to 1.25 after 6 weeks treatment, a decrease of 39.02%. The difference was statistically significant (P < 0.0001, confidence interval [CI] of the difference = 0.54-1.26).[40]

SKIN WHITENING

UV radiation is widely considered as a major cause of skin pigmentation. Upon exposure to UV radiation, the melanocytes increase the production of intracellular nitric oxide, which triggers signal transduction cascades to initiate melanogenesis by tyrosinase. UV radiation also influences melanogenesis through a paracrine regulation process involving the keratinocytes. natural skin whitening products involving tyrosinase blockers like phenols and polyphenols, and non-tyrosinase blockers like α-MSH, melanosome transferase and cytokine inhibitors.[41]

Various gallic acid derivatives of hydroxyflavanols had been is isolated from green tea and some of them were identified as strong tyrosinase inhibitors.[42] Kim et al reported that EGCG and hinokitiol (structurally not related to hydroxyflavanols) were not only tyrosinase inhibitors, but also agents that decreased MITF production in cells.[43] Ellagic acids (EA) polyphenol found in green tea with strong antioxidative properties and tyrosinase inhibition.[44] The skin lightening effects of EA is not fully understood but it may due to chelating copper at the active site of tyrosinase to reduce its activity[45] and inhibition of proliferation of melanocytes and melanin synthesis.[44] In addition, the antioxidative and ROS-scavenging activities of EA may contribute to its skin-whitening effect.

SKIN INFECTION (ANTIMICROBIAL)

When skin is under attack by microbial agents such as viruses or bacteria, it often reacts by local inflammation. Inflammation can also be cause by internal elements such as autoimmune diseases that are associated with damage to the skin, resulting in skin lesions, rash, and altered appearance. Recently, the antimicrobial properties of GTPs have been recognized.[46] Several reports have presented data indicating a strong link between GTPs and prevention of infection by a range of viruses, such as adenovirus[47] Epstein-Barr virus[48] and influenza virus.[49] For skin-related viral infections, C.E. Isaacs et al, study using a cell culture model found that EG CG inactivated HSV.[50] It has been proposed that the antiviral properties of GT Ps are due to their powerful protein binding capacity, resulting in tight binding to the viral coat proteins, and to their ability to modulate the dynamics of the cell plasma membrane, thereby preventing the entry of viral particles into the cells.[51]

ANTIDANDRUFF

As the epidermal layer continually replaces itself, cells are pushed outward where they eventually die and flake off. In most people, these flakes of skin are too small to be visible. However, certain conditions cause cell turnover to be unusually rapid, especially in the scalp. The result is that dead skin cells are shed in large, oily clumps, which appear as white or grayish patches on the scalp, skin and clothes that is popularly known as dandruff.

Green tea naturally exfoliates the dry flakes which are the root of dandruff without dehydrating the skin. The researchers performed tests on an animal model to study the inflammatory skin diseases, characterized by patches of dry, red, flaky skin due to inflammation and overproduction of skin cells. Stefan et al demonstrated that Animals treated with green tea displayed slower growth of skin cells and the activation of a gene controlling the cells' life cycles. Recent green tea and hair research shows that green tea is also good for your scalp. According to a 2007 study conducted by Dr. Stephen Hsu of the Medical College of Georgia, green tea shows promise in treating both psoriasis and its more common cousin, dandruff. Green tea appears to normalize the skin cell growth cycle by regulating a protein called Caspase-14, which tells skin cells when to multiply and when to die off. Green tea has also been shown to soothe skin and reduce inflammation.

GREEN TEA AND HAIR GROWTH

A green tea and hair paper published by scientists at the Saitama Cancer Center Research Institute in Japan noted that green tea suppresses the production of Tumor Necrosis Factor-alpha (TNF-alpha). TNF-alpha has been implicated in androgenetic hair loss (baldness). They noted that consumption of high amounts of green tea increases the amount of sex hormone\converted to dihydrotestosterone (DHT). DHT is a hormone that stimulates hair growth during puberty. According to the American Medical Association, however, some men and women have hair follicles that are genetically programmed to respond negatively to DHT later in life. So, reducing the amount of DHT in the bloodstream could help protect hair follicles in people who have DHT-induced baldness.[52]

Another 2005 study conducted by the Charles R. Drew University of Medicine and Science, Los Angeles used rats as models. 60 female rats experiencing the rat equivalent of baldness were divided into 2 groups. One group was given pure water to drink. The other group was given drinking water that contained a polyphenol extract derived from green tea 33% of the mice who drank the polyphenol-laced water experienced some hair regrowth. Out of the mice assigned to drink water only, none experienced any hair re growth.[53] A 2007 study conducted by the Seoul National University College of Medicine examined the effect of EGCG on hair follicles and dermal papilla cells, a type of cell found in human hair follicles that controls hair growth and plays a role in male pattern baldness.

The Korean researchers tested EGCG on hair follicles cultured in a lab, dermal papilla cells cultured in a lab, and actual human scalps. Compared to control cultures, cultures treated with EGCG showed increased hair follicle

elongation, increased hair growth, and stronger proliferation of dermal papilla cells. The researchers also found specific chemical changes that promoted hair growth in the samples treated with EGCG. Ten percent EGCG in ethanol or ethanol vehicle were applied daily to two regions of the occipital scalp of three normal human volunteer for 4 successive days, and then treated areas about 1 x 1.5 cm were excised. Tissue samples containing hair follicles were cautiously dissected into single hair follicles. Dermal papillae were selectively separated under a stereomicroscope and isolated into single cells for Western blot analysis. According to the researchers, "It was confirmed that the events initially observed in vitro actually occurred in vivo." So, the same chemical changes occurred in human scalps treated using 10% ECGC dissolved in ethanol. Data suggested that EGCG stimulates human hair growth via its proliferative and antiapoptotic effects on DPCs, and may prolong anagen stage. The effects of EGCG on different hair follicle cell types and the molecular basis for its promotion of hair growth remain unclear and require further investigation.[54]

Green Tea is not only a popular drink because of its benefits, but it can be also used for removing stretch marks. Recent research shown, that Green Tea may also be helpful in certain skin complaints as the EGCG found in Green Tea. It helps to rejuvenate dying skin cells. One way in which this may be beneficial is to get rid of stretch marks.

Green Tea may help you with prevention. Dr. Stephen Hsu from Medical College of Georgia Department of Oral Biology has found that the EGCG can cause dying skin cells near the surface of skin, to rejuvenate and start dividing again. Although Dr. Hsu admits that full benefits of this are unknown, he believes that this will help to improve the skin condition. He says that: "If skin cells surrounding wounds or infections don't heal in time, fibroblasts in the connective tissue may rush in to fill the void and cause scar tissue formation. If we can spur the skin cells to differentiate and proliferate, we can potentially accelerate the wound-healing process and prevent scarring." Since stretch marks are caused by tears in the skin and scarring, this property of Green Tea obviously holds great promise for getting rid of stretch marks.[55]

STRETCH MARKS

Table 2: Summary of cosmetological uses of Green tea polyphenols

Photoprotection	Inhibition of UV-induced erythema and Antioxidant effect.	56
Aging and antiwrinkle	Inhibit the activity of collagenase and increases collagen biosynthesis rate of humanfibroblasts.	57
Skin whitening	Tyrosinase inhibition by chelating copper at the site, Decrease MITF production	44, 45 ,58

Skin infection (antimicrobial)	Inhibit influenza virus replication in cell culture and for potentially direct virucidal effect.	59
Hair growth and Hair loss	Suppresses the production of Tumor Necrosis Factor-alpha (TNF-alpha).	60
Antidandruff	Inhibit inflammation, by regulating the expression of Caspase-14, a protein that controls the life cycle of a skin cell.	61

CONCLUSION

Green tea polyphenols becomes one of the favorite ingredients for cosmetic preparations. This brief contribution has discussed a few where human data are available on their skin effects. In general, although the effects may be small, they are significant and do meaningfully improve skin feel and appearance with continued use. For any ingredient to be beneficial it must be stable in production, storage, and use; be nontoxic to the consumer; and have activity at the target site once applied. More study is needed to improve skin penetration of this bioactive cosmetic. Perhaps there is even a need for instrumentation, like ionophoresis for example, to enhance delivery into the skin.

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