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Development of Anti-Acne Gel from Herbal Extraction

S Shanmugapriya[1] (PG Student)
[1]Department of Biotechnology, Sathyabama Institute of Science and Technology, Jeppiaar Nagar, SH 49A, Chennai, Tamil Nadu 600119, India.

T Rajasekar[2] (Assistant Professor- Research)
[2]Department of Centre for Drug Discovery and Development, Sathyabama Institute of Science and Technology, Jeppiaar Nagar, SH 49A, Chennai, Tamil Nadu 600119, India.

S Usha Nandhini[3] (Assistant Professor)
[3]Department of school of Bio and Chemical Engineering, Sathyabama Institute of Science and Technology, Jeppiaar Nagar, SH 49A, Chennai, Tamil Nadu 600119, India.

Abstract:- Acne is a common dermatological issue that affects people all over the world, and it is frequently treated with synthetic medications and chemicals that may have negative effects. Due to their perceived safety and potential usefulness, there has been an increase in interest in recent times in the creation of natural and herbal-based formulations as alternatives to traditional medicines. This paper discusses the creation of anti-acne gels made from herbal extractions and covers the most recent trends and research results in this area. These herbal extracts have a high concentration of bioactive substances, including polyphenols, flavonoids, alkaloids, and terpenoids, which have antibacterial, anti-inflammatory, and antioxidant activities. The herbal extracts showed positive anti-acne effects by inhibiting acne-causing bacteria, lowering inflammation, and scavenging free radicals. A promising approach for addressing this widespread dermatological issue while reducing potential adverse effects related to conventional therapies is the development of efficient and secure anti-acne gels from herbal extractions.

Keywords:- *Acne, Antibacterial, Anti-Inflammatory, Antioxidant, Herbal Extracts.*

I. INTRODUCTION

Sebaceous glands are involved in the chronic inflammatory skin condition known as acne. Androgenic hormone activate increased sebum excessive production, altered follicular keratinization, inflammation, and Propionibacterium acnes are all the results of four primary pathogenesis [1] [2]. Propionobacterium acnes **(**P acnes*)* populate the follicular duct and grows, converting sebum into irritating triglycerides that likely aid in the onset of inflammation. When lymphocytes infiltrate the follicular epithelium, it splits, releasing oil, microorganisms, and keratin into the dermis [3].

It's additionally impacted by foreign matters, impurities, social environment, nutritional and lifestyle, such as worsening air pollution, sweets consumption, to continue to awake for long period of time [4].

One of the most common skin problems among the youngsters is acne [5-7]. Acne normally begins during adolescence and gradually goes away by the time a person is 20 years old, while some people continue to experience acne well into their 40s and 50s [8-12]. According to the Global Burden of Disease Study 2010, acne vulgaris (also known as acne) is the eighth most prevalent skin condition worldwide, with an estimated prevalence (for all ages) of 9.38% [13]. The prevalence of acne varies across nations and age groups, with estimates ranging from 35% to nearly 100% of adolescents having acne at some point [14]. Acne prevalence increased by 5.1% from 2006 to 2016 [15]. Meanwhile, in the US, the average cost of an individual receiving an acne therapy for seven months that was approved by the US Food and Drug Administration [16]. Acne sufferers have been burdened financially as a result of its high prevalence and recurrence. Additionally, although acne is not a life-threatening condition, it can harm a person's look and, if left untreated, can cause scars and marks. Discosmetic dermatosis can also easily result in inferiority for youngsters, which can even hinder their ability to get employment and get married. In a Chinese study, 30.8% of acne sufferers claimed that their condition had a negative impacts [17].

II. CLINICAL FEATURES OF ACNE

Acne's clinical symptoms are a collection of symptoms connected to enlarged, inflammatory, or scarred pilosebaceous units. The primary characteristic is lesional polymorphism, which is most frequently observed on the chest, back, and face. The symptom that manifests the most frequently is seborrhea, Pustules, papules, nodules, and cysts are the many types of inflammatory lesions that can appear on distended pilosebaceous units, which can appear as open or closed comedones. In more extreme situations, a number of blister and lumps and bump combine to form draining sinuses, that cause chronic scarring and, in rare circumstances, malignant alterations [18].

Macular pigmentation and scars (hypertrophic, keloids, ice pick scars, depressed fibrotic and atrophic macules, perifollicular elastolysis) are characterized of post-inflammatory lesions that can also developed. In skin with pigment, post-inflammatory hyperpigmentation is frequently observed [19].

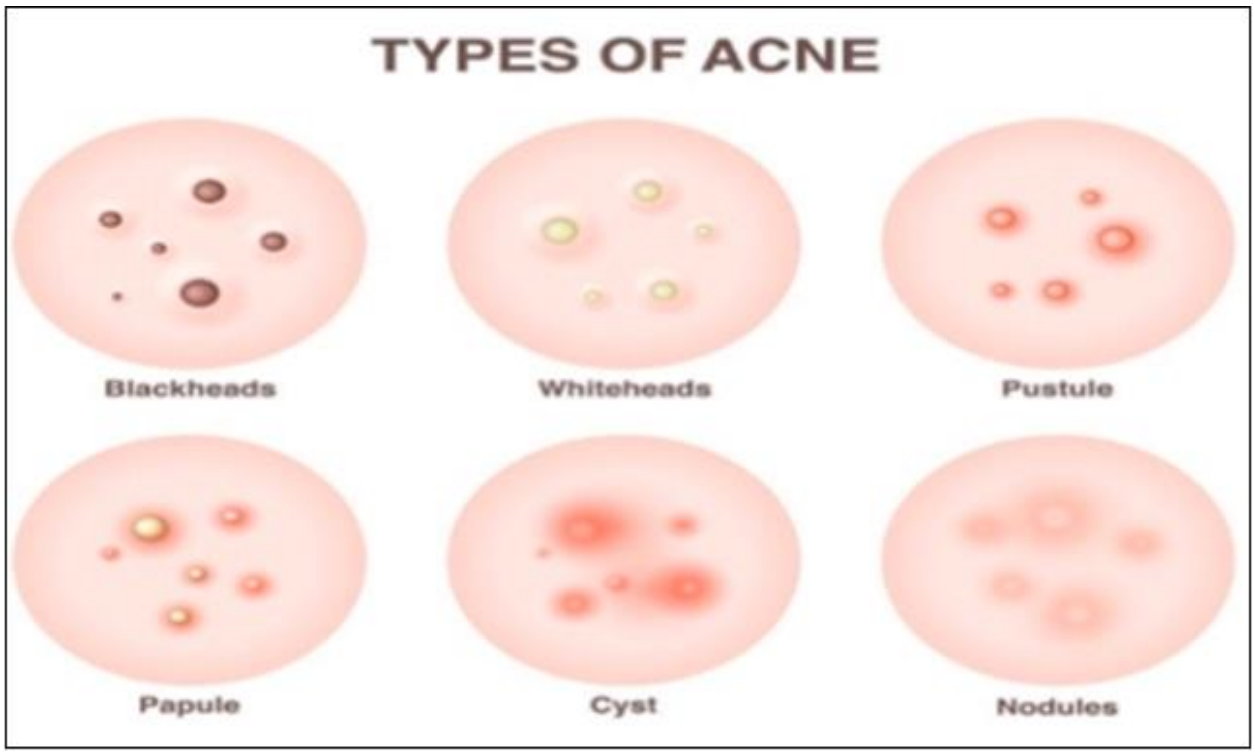

Fig 1 Types of Acne

III. PATHOGENESIS OF ACNE

The pathogenesis of acne is presently trait to a number of causes, including, Increased sebum production, Altered sebum lipid quality, Androgen activity, Proliferation of Propionibacterium acnes (P. acnes) within the follicle, and follicular hyperkeratinization [20].

➢ *Increased Sebum Production*

Acne is a condition whose development is aided by increased sebum secretion. Sebaceous glands create neutral and polar lipids, plays a number of different parts in signal transduction and are connected to biological path. Increased sebum production lead to oily skin or acne [21].

➢ *Altered Sebum Lipid Quality*

Fatty acids also function as ligands for nuclear receptors like PPARs. While sebocytes stimulation of the 5-lipoxygenase and cyclooxygenase-2 pathways results in the generation of pro-inflammatory lipids, sebaceous gland lipids have direct pro- and anti-inflammatory effects [22].

➢ *Androgen Activity*

Sebaceous gland size and sebum release are also regulated by hormones like androgens. Androgens simply encourage sebocyte proliferation in cell culture, but PPAR ligands are necessary to induce differentiation and lipogenic activity [23].

➢ *Proliferation of Propionibacterium Acnes within the Follicle, and Follicular Hyper Keratinization*

On the other hand, P. acnes may activate keratinocytes and sebocytes through TLR, CD14, and CD1 molecules [24]. Acne lesions contain macrophages that have TLR2 expressed on their surface around the sebaceous follicles. TLR2 activation causes the transcription nuclear factor to be triggered, which in turn causes the synthesis of cytokines and chemokines, a phenomenon seen in acne lesions. Additionally, P. acnes causes the release of IL-8 and IL-12 from TLR2 positive monocytes [25].

Above circumstances provoke the follicular rupture, infrainfundibular inflammation, and creation of the perifollicular abscess, all of which provoke the wound healing process. A series of wound healing events are triggered by skin injury. One of the most intricate biological processes is wound healing, which includes extracellular matrix components, soluble chemical mediators, as well as infiltrating blood cells.

Atrophic or hypertrophic marks and scars can develop at the area of tissue damage. Inflammation, Granulation tissue development, and Matrix re-modelling are the three steps of the healing process for wounds [26, 27].

- *Inflammation*

After vasoconstriction for hemostasis, blanching happens. Vasoconstriction is replaced by vasodilation and subsequent erythema once the blood flow has been interrupted. Additionally, melanogenesis might be induced.

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This procedure is crucial for the emergence of postacne erythema and hyperpigmentation. Activated blood cells such as granulocytes, macrophages, neutrophils, lymphocytes, fibroblasts, and platelets release inflammatory mediators that prepare the area for the creation of granulation tissue [28].

The irritant response at the pilosebaceous gland was well built and lasted in patients with marks versus those without; in addition, the inflammatory reaction was deliberate in patients with marks, according to research by Holland et al. on biopsy specimens of acne lesions from the back of patients with presence of marks and in the absence marks. They demonstrated a significant correlation between the intensity and length of inflammation and the emergence of scarring, indicating that the best method for preventing acne scarring may be to treat early inflammation in acne lesions [29].

- *Granulation Tissue Development*

New capillaries grow while damaged tissues are healed. In place of neutrophils, monocytes undergo a transformation into macrophages and release a variety of growth factors, such as platelet-derived growth factor, fibroblast growth factor, and transforming growth factors and, which promote fibroblast migration and proliferation [30]. About 3 to 5 days after the wound has formed, fibroblasts start to produce new collagen. Early on, type III collagen predominates in the new skin's composition, with only a tiny amount of type I collagen (20%). However, in mature scars, the mix of collagen types changes to resemble that of unwounded skin, with about 80% of type I collagen [31].

- *Matr Remodelling*

The extracellular matrix metalloproteinases (MMPs) and tissue MMP inhibitors are produced by fibroblasts and keratinocytes, respectively. MMPs are extracellular matrix (ECM) destroying enzymes that work together to produce a lytic cascade for ECM remodeling [32]. As a result, atrophic or keloids can form when there is an imbalance between the amount of MMPs and tissue inhibitors of MMPs. If the healing reaction is excessively enthusiastic, a raised nodule of fibrotic tissue occurs in the formation of hypertrophic scars. Inadequate response causes reduced deposition of collagen components and an atrophic scar [33].

IV. TYPES OF ACNE SCAR

➢ *Damage to the Skin During the Recovery of Aggressive Acne can Lead to Scarring. Scars can be Classified into:*

- *Atrophic*
- *Hypertrophic*

Based on the net loss or gain of collagen. In comparison to a few who exhibit hypertrophic scars and keloids, 80–90% of patients with acne scars have scars connected to a loss of collagen (atrophic scars).

➢ *Atrophic Scar*

In a ratio of 3:1, atrophic acne scars are more prevalent than keloids and hypertrophic scars. They have been divided into

- *Ice Pick,*
- *Boxcar, and*
- *Rolling Scars.*

When it comes to atrophic scars, the ice pick type accounts for 60%–70% of all scars, the boxcar type for 20%–30%, and rolling scars for 15%–25%. [34].

- *Ice Pick*

Deep, punctiform, and thin (2 mm) scars are referred to as icepick scars. This kind of scar often has an aperture that is larger than the deeper infundibulum and forming of “V" shape.

- *Boxcar*

Boxcar scars are rounded or oval scars with distinct vertical edges. These scars do not have the tapering V form and are typically wider at the surface than icepick scars. Instead, they can be seen as a wide-base "U" shape. Boxcar scars can be light or heavy.

- *Rolling Scar*

Rolling scars are characterized by dermal tethering of the dermis to the subcutis and are typically wider than 4 to 5 mm. These scars give the skin a "M"-shaped look that is rolling or undulating [35][36].

➢ *Hypertrophic*

Scars that are hypertrophic and keloidal tend to have excessive collagen buildup and reduced collagenase activity. Typically pink, elevated, and hard. Hypertrophic scars have a comparable histology to normal dermal scars. Keloids, on the other hand, develop as reddish-purple papules and nodules that spread over the boundaries of the initial lesion and are histologically distinguished by thick bundles of hyalinized acellular collagen grouped in whorls. Darker skinned people are more likely to have hypertrophic and keloidal scars, which mostly affect the trunk [37].

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V. HERBAL TREATMENT FOR ACNE

Due to their benefits, including improved patient tolerance, with no side effects, and being less expensive, herbal treatment are becoming more and more popular [38]. Acne and other infectious disorders are treated in various ways using a variety of medicinal herbs with anti-inflammation and antibacterial properties [39] [40].

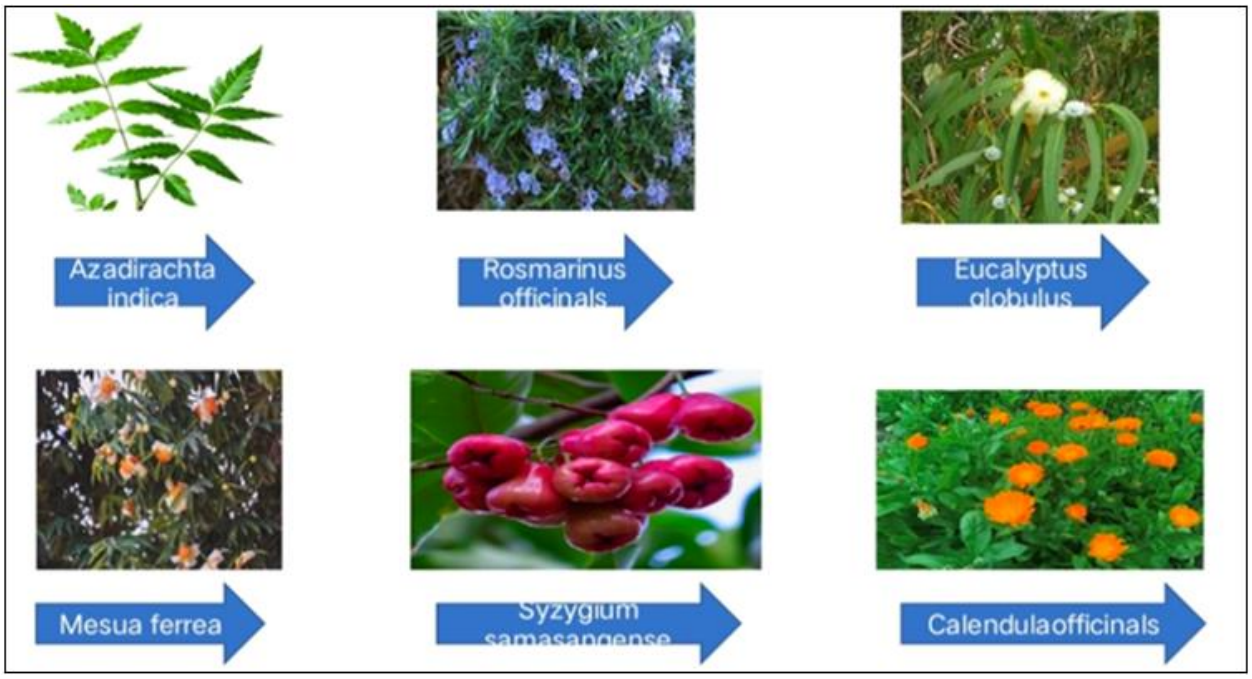

Fig 2 Herbal Plants for Treatment of Acne

➢ *Azadirachta indica*

A member of the Meliaceae family, neem (Azadirachta indica) has medicinal implications for the prevention and treatment of infection. As a high source of antioxidants and other beneficial active substances like azadirachtin, nimbolinin, nimbin, nimbidin, nimbidol, salannin, and quercetin, it is thought that Azadirachta indica has medicinal properties. Parts of the neem (Azadirachta indica) plant exhibit an antibacterial function by inhibiting microbial growth and/or the capacity for cell wall collapse [41]. An ethanol extract of *Azadirachta indica*, *G. glabra*, *Andrographis paniculata*, *Ocimum sanctum*, and green tea was found to have the capacity to inhibit acne in an investigation on an anti-acne formulation made from herbal extracts. In this investigation, Propionibacterium acnes and Staphylococcus epidermis were successfully eradicated by the anti-acne formula [42]. Azadirachta indica leaf aqueous extract has the potential to be chemo preventive against mouse skin carcinogenesis.

Proliferating cell nuclear antigen expression has been found to be higher in skin cancers than in the control group. Skin cancers in this investigation have substantial levels of lipid peroxidation [43].

➢ *Rosmarinus officinalis*

A common houseplant that is grown all around the world is Rosmarinus officinalis. It is employed in cosmetics, culinary flavoring, and beverages. Rosmarinic acid can be found in Rosmarinus officinalis. Photo-cancers and photo-aging are manifestations of chronic UV exposure. Due to its antioxidant activity, R. officinalis aqueous extract is beneficial in preventing photo damage brought on by UV radiation [44]. Among the phenolic chemicals discussed, rosmarinic acid and carnosic acid have the most anti-inflammatory and antioxidant properties [45, 46]. Oxidative stress and infections are related. Therefore, regardless of their antibacterial activity, the substances with antioxidant properties may be advantageous in this approach. Additionally, Rosmarinus officinalis oil has shown promise in the fight against the acne-causing acnes bacteria. In research, the antibacterial effects of Rosemary essential oil were assessed against acnes, and it was found that the therapy had a substantial impact on the size and morphology of the bacteria [47].

➢ *Eucalyptus globulus*

The Myrtaceae family includes the species Eucalyptus globulus. This plant's essential oil is utilized extensively worldwide for a variety of items, including food, cosmetics, fragrances, and pharmaceuticals. It has been observed that the oil contains antibacterial, anti-inflammatory, and antioxidant properties [48]. It exhibits antibacterial properties against a variety of microorganisms, and although the precise mechanism of action is unknown, a number of theories have been proposed, including the capacity to damage cell walls and membranes, which would cause ATP and metabolite leaks. Additionally, because the oil is hydrophobic, it increases cell permeability, which causes bacterial cells to leak [49]. *Eucalyptus globulus* is a well-known shrub with enormous therapeutic value. Numerous species of eucalyptus have also received extensive research into their potential therapeutic benefits [50].

Six gram-positive bacteria, including *Propionibacterium acnes, Staphylococcus aureus, Enterococcus faecalis, Bacillus cereus,* and *Alicyclobacillusacido terrestris*, as well as fungi, were able to proliferate less when *Eucalyptus globulus (*Tasmanian Bluegum*), E. maculata* (Spotted Gum*), and E. viminalis* (Manna Gum) were present [51] [52]. Propionibacterium acnes and other bacteria are resistant to the antibacterial effects of eucalyptus essential oil **[**53] [54**].**

- *Mesua ferrea*

Mesua ferrea, sometimes referred to as Nageswar or Nagkesar locally, is one of the oldest medicinal plants and has great cultural significance. The plant is a member of the family Guttiferae. It has about 100 species spread throughout 47 genera. This family includes the well-known genera Cratoxylum, Hypericum, Garcina, Mesua, and Vismia [55][56]. Following a chemical analysis of this plant, ligans, alkaloids, flavonoids, tannins, phthalic acid, gallic acid, and terpenoids were among the compounds that were recognized. Melaferrone-A and B, mesuaferrol, mesuanic acid, α-and β-amyrin, and β-sitosterol found in stamen are the main components of Mesua ferrea Linn [57]. Another study found that *Mesua ferrea* flower extract was effective against five distinct strains of Salmonella spp. When the extract was diluted to 50 µg, it was discovered to be effective against every strain. Furthermore, floral extract reduced the viable count of bacterial strains in liver, spleen, and heart blood at a dose of 2-4 mg/mouse and had encouraging in vivo antibacterial activity in S. Typhimurium NCTC 74 challenged mice [58]. In the early in vitro anticancer screening tests, a number of crude extracts and purified compounds have demonstrated encouraging anticancer properties. With an IC50 value of 12.5 µg/ml, the volatile oils-rich methanol extract of Mesua ferrea flowers demonstrated potent cytotoxic effects against T-lymphocyte leukemia cells [59].

- *Syzygium samasangense*

Wax apple, or jambu air madu, is known as *Syzygium samarangense*. It's a nonclimacteric tropical fruit belonging to the Myrtaceae family [60].

Fruit pulp contains a high concentration of phenolics, flavonoids, and other antioxidant chemicals, it is thought to offer significant potential health advantages. It has been used in traditional medicine to treat a range of diseases and ailments in addition to being consumed as food. Astringent, carminative, diuretic, antibacterial, antiscorbutic, and in deal with treatment high blood pressure and a variety of inflammatory diseases, inclusive of sore throats [61]. Moneruzzaman et al. (2015) state that the phytochemicals—such as anthocyanin, flavonoids, phenolic acid, and tannins—found in the extract of Syzygium samarangense are what protect against microbial infection. In addition, because Syzygium samarangense may heal irritated skin, it is also used to treat skin infections [62].

- *Calendula officinals*

Asteraceae's Calendula genus contains about twenty-five herbaceous annual or perennial species. The most common species include *Calendula officinalis Linn., Calendula arvensis Linn., Calendula suffruticosa Vahl., Calendula stellata Cav., Calendula alata Rech., and Calendula tripterocarpa Rupr* [63]. The herb *C. officinalis Linn*., sometimes known as pot marigold, has long been used to treat internal organ inflammations, gastrointestinal ulcers, dysmenorrhea, and seizures by acting as a diuretic and diaphoretic. It is also used to treat burns, wounds, and inflammations of the pharynx and oral mucosa [64]. The antipyretic, anti-tumor, and cicatrizing properties of the dried flower heads have been utilized [65]. There is some evidence that calendula Officinalis can significantly reduce grade 2 or greater skin toxicity in women undergoing breast irradiation [66]. Calendula has an impact on the skin's structure as well. Akhtar et al. used a cutometer to measure skin distensibility, viscoelasticity—a measure of the water content of the epidermis and dermis—and direct markers of skin firmness. They discovered that calendula significantly improved these parameters [67] [68].

Table 1 Herbal Plants and its Significant Components

S.no	Family Name	Common Name	Scientific Name of the Plant and Fruit	Significant Components
1	Meliaceae	Neem	*Azadirachta indica*	Nimbolinin, nimbin, nimbidin, Nimbidol, salannin, and quercetin.
2	Lamiaceae	Rosemary	Rosmarinus Officinalis	Carnosic acid and rosmarinic acid
3	Myrtaceae	Tasmanian bluegum	Eucalyptus globulus	Ester's monoterpene, aldehydes, and ketones and sesquiterpenes
4	Calophyllaceae	Ceylon ironwood	Mesua ferrea	Xanthones, triterpenoids, and flavonoids
5	Mystaecae	Java apple	Syzygium samasangense	Flavoonoiids ,flavanonus,anthocyanosides, and terpenoids
6	Asteraceae	Pot marigold	Calendula officinals	Carotenoids triterprnic, flavonoids

VI. CONCLUSION

Herbal and medicinal plants have been used for a long time and have been found to have little adverse effects. These plants are a dependable source for creating novel medications. A number of plants appear to prevent the development of bacteria, fungus, and viruses. Additionally, certain plants have showed anti-bacterial and anti-inflammatory effects. Acne can be treated using a variety of various methods using medicinal plants and herbs. There are a limited number of clinical studies signify the efficacy and therapy of acne like problems.

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