APPENDIX 1

FLAVONOID DERIVATIVES USED TO TREAT ACNE

Project Report submitted in partial fulfillment

for the award of the degree of

BACHELORS OF PHARMACY

Submitted by

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APRIL/MAY 2020-21

APPENDIX 2

SCHOOL OF MEDICAL AND ALLIED SCIENCES

BONAFIDE CERTIFICATE

Certified that this project report **"FLAVONOID DERIVATIVES USED TO TREAT ACNE"** is the bonafide work of **"SHLOK KUMAR (1712102085)** who carried out the project work under my supervision.

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SIGNATURE OF SUPERVISOR
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Approval Sheet

This thesis/dissertation/report entitled ‘flavonoid derivatives used to treat acne’ by Shlok kumar is approved for the degree of Bachelors in Pharmacy

Examiners

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Supervisor (s)

_____

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Chairman

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Date: _____

Place: _____

Statement of Project Report Preparation

Thesis title: Flavonoid Derivatives used to Treat Acne

1. Degree for which the report is submitted: Bachelors in Pharmacy.
2. Project Supervisor was referred to for preparing the report.
3. Specifications regarding thesis format have been closely followed.
4. The contents of the thesis have been organized based on the guidelines.
5. The report has been prepared without resorting to plagiarism.
6. All sources used have been cited appropriately.
7. The report has not been submitted elsewhere for a degree.

Signature of Student:

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Statement of Preparation:

Every student has to submit the statement of thesis preparation

ABSTRACT

Acne is a skin condition that happens when oil and dead skin cells clog our hair follicles. It triggers pimples, blackheads, and whiteheads. It typically begins when adolescent is thirteen years old, but it is not age-based. Acne is a chronic condition, but there are successful treatments available in today's society. It appears out of nowhere and heals slowly. Acne leaves dark spots and scars on the skin long after it heal, causing emotional stress. Fruit, flowers, vegetables, and seeds contain flavonoids, which are polyphenolic compounds. Flavonoid aids in cellular activity regulation and protects against radicals that induce oxidative stress in our bodies. Both are linked to antioxidant benefits and the slowing of drug metabolism. The mechanism of action of six different forms of flavonoids that aid in the treatment or prevention of acne is detailed in the paper. Acne is treated with cosmeceuticals and antibiotics, in addition to naturally occurring flavonoids.

Keywords: Acne, Treatment, Flavonoids, Antibiotics, Prevention, Cosmeceuticals, Skin, Metabolism, Drug, Against, Chronic, Disease.

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CHAPTER 1. INTRODUCTION

FLAVONOIDS IN TREATING ACNE

Acne is a skin condition caused by oil and dead skin cells clogging our hair follicles. Blackheads, whiteheads, and pimples are all caused by acne. It usually begins with enlarged facial grease development and mid-facial comedones, accompanied by inflammatory lesions, in early puberty. It commonly starts with the age of adolescent that is thirteen years and is moderate to severe in about fifteen to twenty percentage. Although, it affects people with all age or gender but mostly found among teenagers. Acne is persistent in nature but there are effective treatment is also available in our society. It suddenly pop-ups and heal very slowly and when it seems to be going other seem to crop-up.[1] Even after healing of acne it leaves black spots and scar on the skin which causes mental stress. It varies by skin type, whether oily or rough. Excess oil (sebum production), clogged hair follicles with oil and dead skin cells, bacterial infection, and inflammation are the four major factors that cause acne. Acne can be divided into three classes. The first is Acne Vulgaris, which is an inflammatory skin condition, follicular disorder, which affects hair follicle mostly on faces, neck and upper trunk and is characterized by inflammation, excess sebum production, hypercornification and hyperpropionbacterium. It begins at the age of adolescents, 13onwards. That affects both genders equally.[2] .

Etiology- due to genetic disorder, hormonal misbalance, and family history of acne. Second is, Acne Rosacea: is an inflammatory skin discharge which occurs more often in middle and older adults. It is specified by erythema, macules and pustules. It mostly affect nose that may give burning and itching. Etiology – emotional stress, exposure to extreme cold or hot, and by food items such as tea, caffeine and alcohol. Symptoms- redness, small cyst, red bumps, blazing. And the third, Acne Conglobata: mainly shown in adults and characterized by interconecting abscess and irregular scar. [3] .

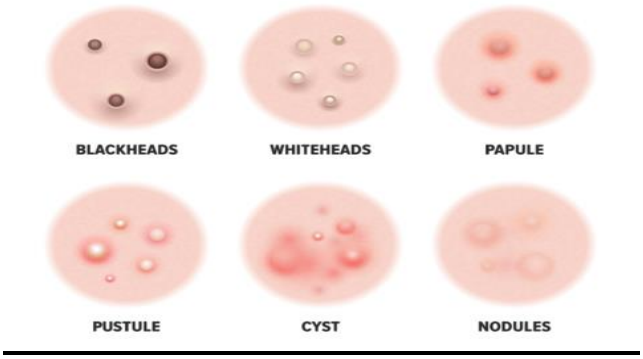


Fig 1:- DIFFERENET TYPES OF ACNE

CHAPTER 2. PREVELANCE AND HISTORY

Since implications of skin aggravation and reality have changed a particularly lot among researches, and considering the way that evaluations are baffled by the openness and utilization of skin break out medicines, it's difficult to see normality measures. Self-nitty gritty skin split out examinations have wind up being mixed up. Skin break out is generally thought to be a high schooler issue, anyway it can last far into adulthood. Skin break out typically begins in early pubescence with an extension in facial oil utilization, mid-facial comedones, and searing bruises. Early phase skin break out (before the age of 12 years) is regularly comedonal rather than provocative, likely in light of the fact that these individuals have not yet started to develop adequate sebum to help tremendous peoples of Proprionic bacterium acnes.[4] .

The subsequent augmentation of the propionic bacterial skin greenery (in the nares and a short time later facial skin) occurred earlier in skin aggravation slanted youths than in skin break out free posterity of a comparative age and pubertal status, exhibiting that delaying sebum improvement or the advancement of the propionic bacterial skin verdure until after pubescence could hinder skin break out or diminish disease earnestness.[5] Early phase of comedonal skin irritation and a creating number of family members with a foundation set apart by skin break out are the two markers of skin aggravation earnestness.[6] .

The female cycle, picking, and mental pressing factor a few the 14 factors that can make skin irritation emit. Outside factors causing skin irritation are seen differently by different ethnic social affairs. Skin irritation vulgaris is a determined skin condition that can continue to go for a serious long time. Inescapability all together Our current appreciation of the trademark history of skin aggravation relies upon examinations of various masses that show a steady abatement in skin irritation recurrence after the age of 20 years.[7]

In a huge degree of youngsters with skin break out, delicate provocative skin break out improves or disappears. Cytokines that cause comedogenic changes at the follicular infundibulum can similarly prevent sebaceous organ lipid release, making solitary wounds evaporate. Seborrhoea, on the other hand, will last well into adulthood, well after the combustible wounds have recovered. Grown-up skin irritation actuated by flowing androgens is generally called post-youthful grown-up skin aggravation or late-starting skin break out and happens most customarily in women past the age of 25 years. [8] .

Acne causes actual side effects like touchiness, irritation, and inconvenience; however its primary impact is on one's personal satisfaction. Mental dismalness is a significant issue and it is exasperated by an assortment of elements: Acne influences exceptionally obvious skin, which is an essential organ of social showcase; standard culture and social pressing factors require wonderful skin; medical services professionals excuse skin break out as a minor self-restricting condition;

Acne is generally basic during youth, when trust and confidence are generally significant. Skin inflammation seriousness and mental problem don't generally compare—gentle infection can cause significant degrees of mental inability in one individual, though more genuine sickness can cause another to appear to be less troubled by their acne. [9] .

Flavonoids are polyphenolic compound which are found in fruit, flowers, vegetable and seeds. Flavonoid assists in regulating cellular activity and prevents from radical that causes oxidative stress in our body. If we put it in simple term, they help our body characteristic more accurately whilst protecting ir towards everyday toxins and stressors.[10] .

Flavonoids are additionally effective antioxidant agent. There are 6 primarily different types of Flavonoids that are: - Flavones, Anthocyanidins, Flavonones, Isoflavones, Flavonols, Flavanonls. Flavones: These consist of Luteolin and apigenin. Celery, Parsley, hot peppers and different kind of herbs are good sources of flavones. Both are linked to antioxidant benefits and the slowing of drug metabolism.[11] .

Malvidin, pelargondin, peoidin, and cyanidin are examples of anthocyanidins. Anthocyanidins can be found in purplr, red, and blue berries, plums, pomegranates, red and purple grapes, and red wine. Flavonones: These consist of hesperetin, eriodictyol and naringenin. Citrus fruits are good sources of flavonones. These are linked to cardiovascular health, relaxation, and anti-inflammatory and antioxidant function.[12]

Genistein, glycitein, and daidzein are isoflavones. Isoflavones can be found in soybeans, soy products, and legumes. These are phytoestrogens sometimes they act as antioxidant and sometimes as oxidant. Thatswhy there effect on cancer is notclear. Flavonols: Thses Flavonoids include quercetin and kaempferol. Flavonols can be found in onions, leeks, Brussels sprouts, broccoli, tomatoes, apples, tea, beans, and kale.[13] . It is likewise known to have mitigating impacts. Kaempferol and other flavonols have been connected to calming and cell reinforcement properties that help to forestall constant illness. Flavanols are divided into three categories: monomers, dimmers, and polymers. Flavanols can be found in cocoa, beans, tea, apples, fruit, grapes, red wine, and fava beans.[14] Green and white teas contain a lot of monomers. Monomer is also linked to heart, circulatory, and neurological health. Dimmers have been linked to a reduction in cholesterol level.

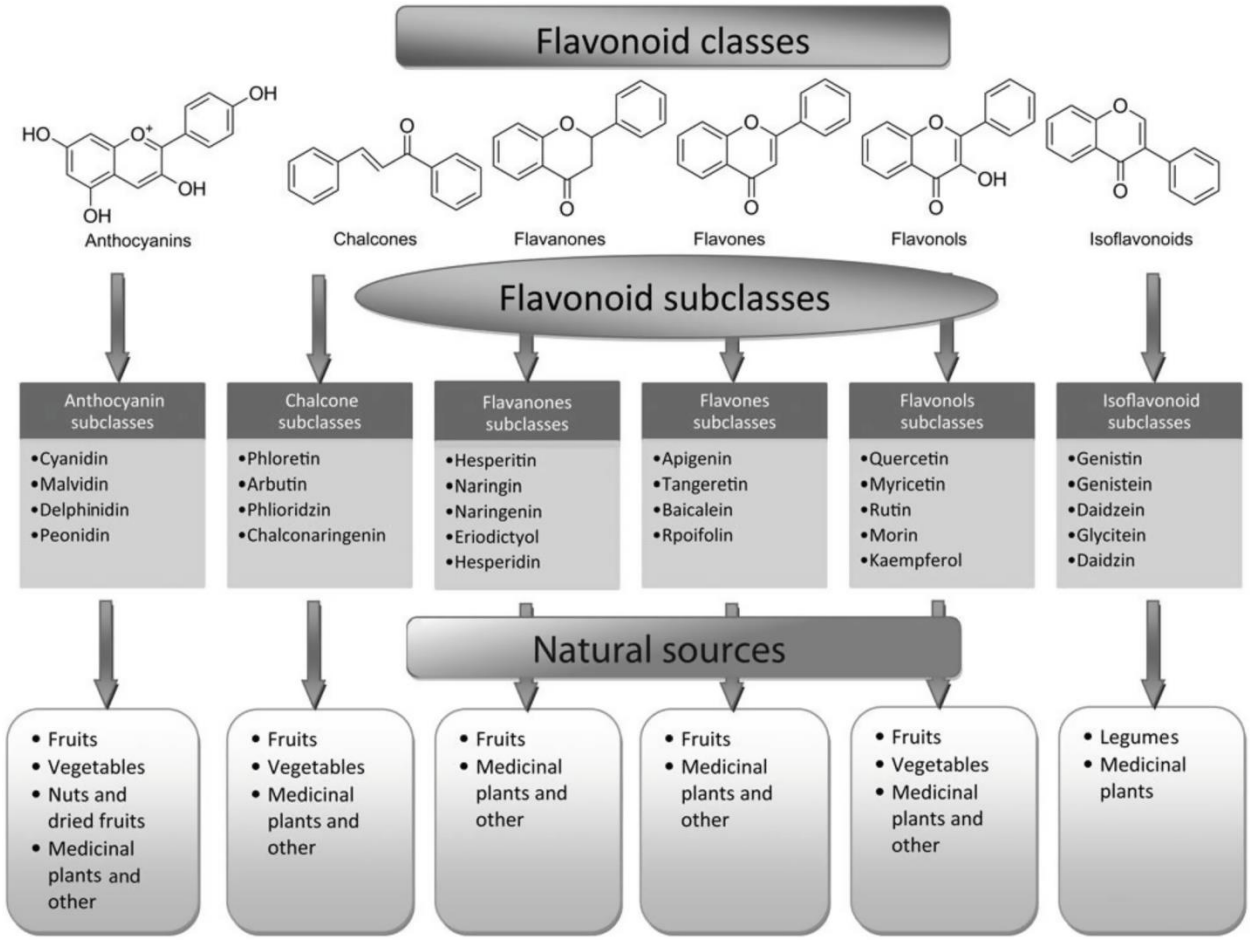


TABLE 1: FLAVONOIDS CLASS

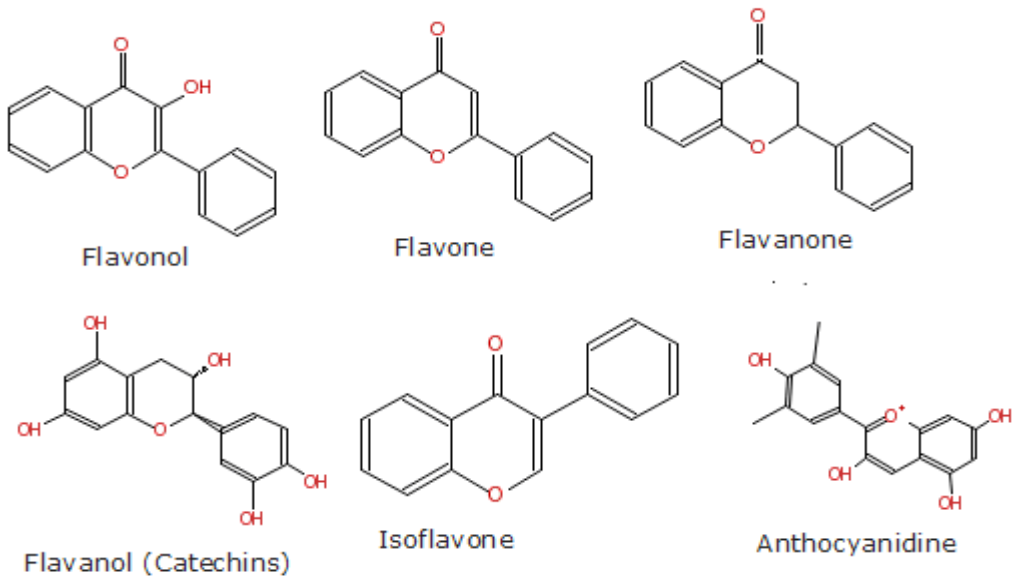


FIG 2:- TYPES OF FLAVANOIS

Sub class	Dietary flavonoid	Common food sources
Anthocyanidins	Petunidin, Peonidin, Pelargonidi, Delphinidin, Cyanidin	Blue, Purple, and Red berries Purple and Red grapes Red wine
Flavones	Baicalein, Luteolin,Chrysi, Apigenin	Parsley, Hot peppers Thyme, Celery
Flavan-3-ols	Proanthocyanidins Theaflavins, Thearubigins Catechin, Epicatechin, Epigallocatechin, Gallocatechol and their gallate derivates	Oolong tea, white tea, green tea, and green tea Cocoa-based products Grapes, berreies, apples, red wine
Flavanones	Eriodictyol, Hesperetin, Naringenin	Citrus fruit and juices(organs, lemons, grapefruits)
Flavonols	Isorhamnetin, Kaempferol, Qercetin, Myricetin	Onions, spring onions, apples, broccoli, kale, berries, teas
Isoflavones	Daidzein, Glycitein, Bichanin A, Genistein, Formononetin	Soy foods, Soybeans, Legumes

TABLE 2: SOURCES OF FLAVONOIDS

General Method of Extraction of Flavonoids:-

Powdered plant material extracted with various solvent according to types of flavonoids such as Isoflavones, Flavonals , Flavanones. Less polar flavonoids extracted with non-polar/less polar solvents (chcl3, diethylether, ethylacetate). While more polar flavanoids extracted with alcohol or aqueous alcohol (flavonoid glycoside).

Fraction of alcoholic extract with ethyl acetate separate most of semi-polar flavanoids from mixture.

Column chromatography – Non polar Flavanoids.

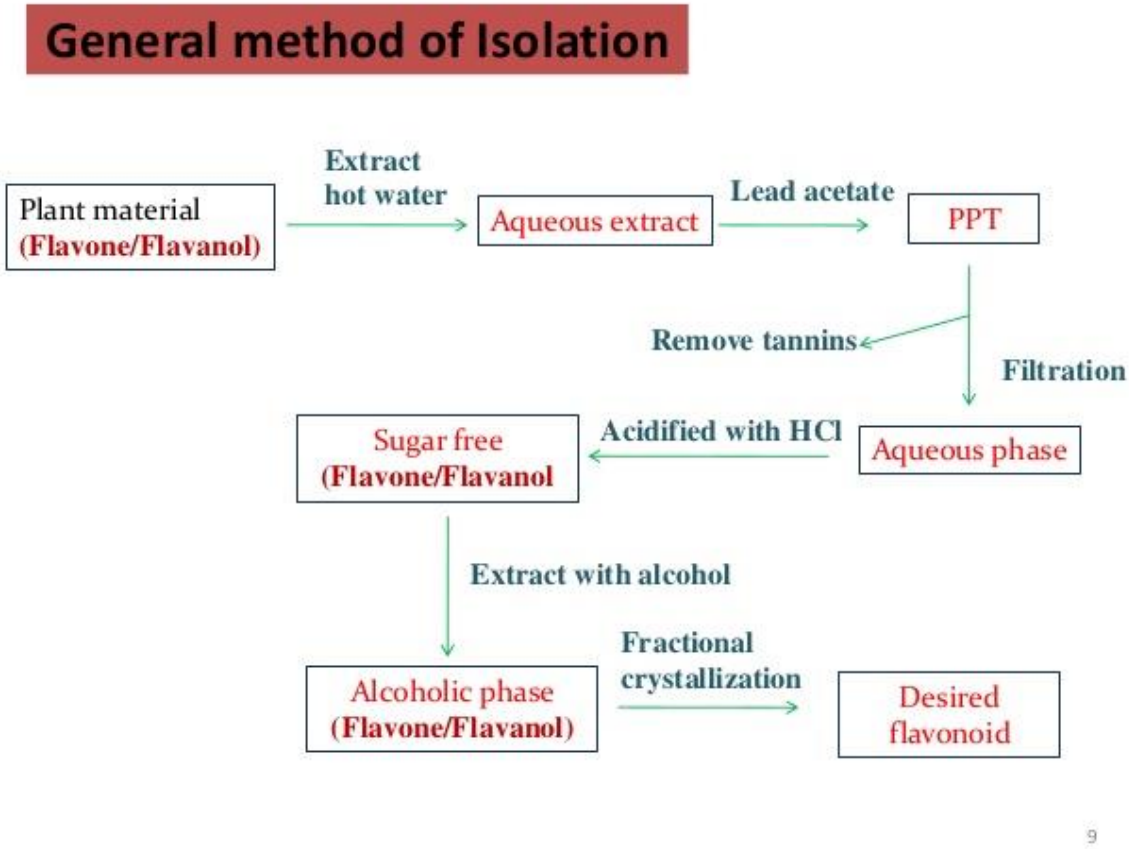


TABLE 3: ISOLATION OF FLAVONOIDS

Identification Test of Flavonoids:

1. Shinoda test – Test solution + few magnesium burning + Concentrated HCL dropwise → give pink scarlet, crimson red colour, occasionly green.
2. Alkaline reagent test – Test solution +Aqueous NAOH solution
   ↓
   Intense yellow colour
   ↓ (few drop of dilute acid)
   Colourless (yellow colour disappear)
3. Aqueous alcoholic solution of flavonoids + Aqueous NAOH solution
   Anthocyanin →Blue to violet colour , Flavones and flavonol →deep in colour , chalcones and aurones →Red to purple colour , Flavonones →colourlesss to yellow colour on heating gives deep red colour .
4. Ferric chloride test →Test solution + Ferric chloride aqueous solution →Green , purple to brown colour.
5. Lead acetate test →Aqueous alcoholic solution + aqueous alcoholic solution + Lead acetate solution →yellow to deep red colour ppt (flavones) ,deep orange red colour (aurones , chalcone).
6. Aqueous alcoholic solution of flavonoids + Dilute sulphuric acid →orange –crimson colour , Intensly yellow/orange solution (anthocyanin,flavones,flavonols).

Chemistry of flavonoids:-

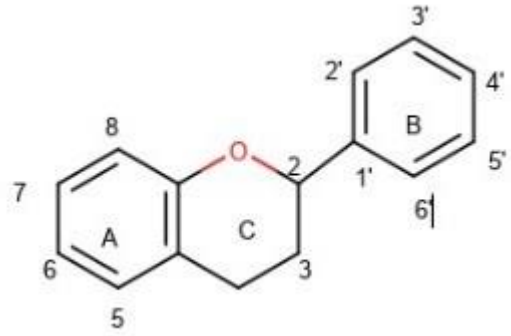


Fig 3: FLAVONOIDS

- **S.A.R of flavonoids** –

General strucure of flavonoids that usually contain hetrocyclic ring which is Benzopyan (oxane containing ring) in which benzene is fused with pyran.
At 2nd position we observe the phenyl ring that will attached with the side chain now this is the general structure of the flavonoids which can be modified at the different for example one of the important modification is the change in the location of phenyl ring now here we can observe that that the phenyl ring attached to the main chain t the 2nd position but this phenyl ring can also be present at the 3r position where they are also called as flavonoids but they are isomers of these flavonoids so we have to use the prefix `iso` so they are commonly known as isoflavonoids.
Similarly other modification are saturation of double bond Between the 2nd and 3rd carbon an introduction of ketone or OH group at 4th position and substitution of the OH group at the different position on the phenyl rings by all of these modification we can observe so many types of flavonoids which are present in the various types of plants .

1. Flavone: It contain Ketone group at 4th position that's why they are having suffix one and the basic ring system is flavonoids so the prefix flav so it commonly called Flavone.

Flav + one → Flavone
There are 4 different types of flavone such as:

- Chrysin = 5,7- dihydroxy

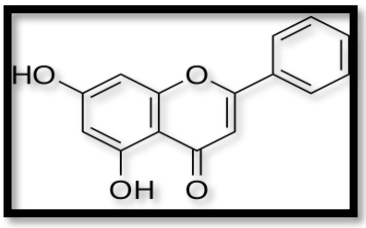


Fig 4: Chrysin

- Apigenin = 5,7,4'- trihydroxy

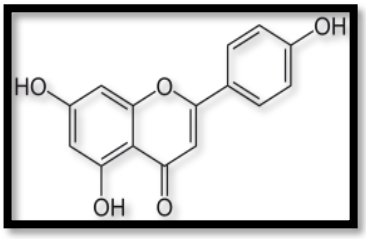


Fig 5: Apigenin

- Leuteolin = 5,7,3',4'- tetrahydroxy

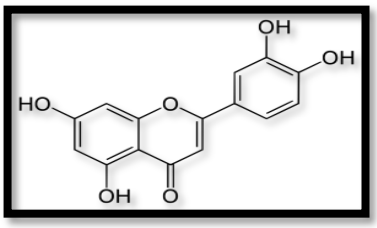


Fig 6: Leuteolin

- Tricetin = 5,7,3',4',5'- pentahydroxy

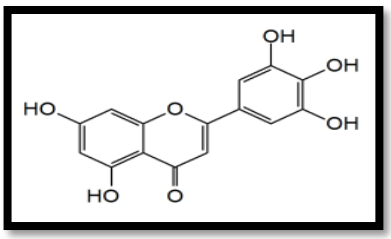


Fig: 7 Tricetin

2. Flavonol : It contain hydroxyl group at the 3rd position now they are having both ketone at the 4th position and OH group at the 3rd position . So that's why we can compile the name as Flavonol.
Flav + one + ol → Flavonol.
Different types of flavonol are :

- Kaempeferol = 3,5,7,4'-tetrahydroxy

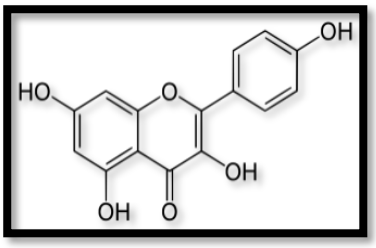


Fig 8: Kaempeferol

- Quercetin = 3,5,7,3',4'-pentahydroxy

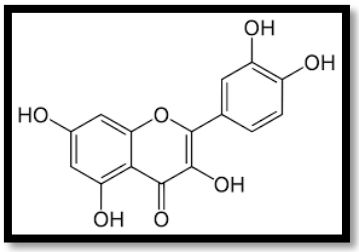


Fig 9: Quercetin

3. Isoflavone:- It contain phenyl group at 3rd position while in all other flavonoids phenyl ring is present at the 2nd position.
Iso + flav+ one →Isoflavone

- Types of isoflavone are –
- Daidzein= 7,4'-dihydroxy

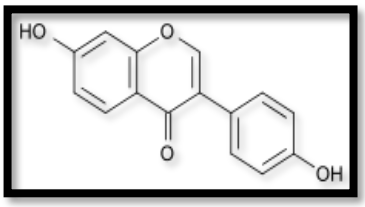


Fig 10: Daidzein

- Genistein= 5,7,4'-trihydroxy

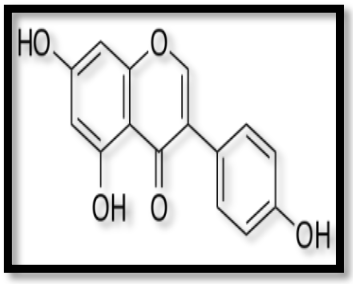


Fig 11: Genistein

4. Flavanone:- At 2nd and 3rd position there is a saturation that's why the name is some what modified now the name is;
Flav+ane +one →Flavanone.
Types of Flavanones –

- Naringenin = 5,7,4'-trihydroxy

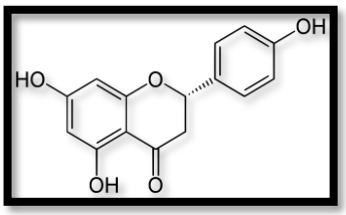


Fig 12: Naringenin

- Hesperitin= 5,7,3'-trihydroxy-4'-methoxy

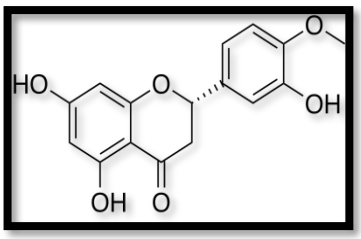


Fig 13: Hesperitin

5. Flavan-3-OL:- Here we observe saturation between 2nd and 3rd carbon and extra OH group at the 3rd position so now the name is Flav+ane+3-OL→Flavan-3-OL

- Quercetin= 3,5,7,3',4'-pentahydroxy flavan

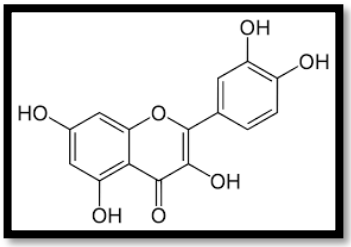


Fig 14: Quercetin

6. Anthocyandins:- OH group at the 3rd position and an extra double bond says that they are forming a oxonium ion now they are made up of Flavyl ring system and the positive charge on the oxygen can be represented with the suffix ium. So this ring is nothing but the Flavyl+ium→Flavylium.

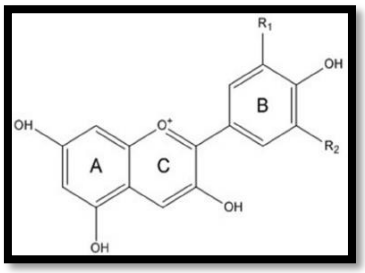


Fig 15: Anthocyandins

Anthocyandins are flavylium ring system where auxim is getting the positive charge. So this is one of the structure cyanidin. cyanidin is just like the quercetin its angular OH group at the 3,5th and 7th position as well as another OH group at 3rd position and 4th position on the phenyl ring but it is a cation with a positive charge on th oxime so cyanidin is 3,5,7,3',4'-pentahydroxy flavylium

CHAPTER 3. LITERATURE REVIEW

❖ FLAVONOIDS IN TREATING ACNE:

- Acne vulgaris pathogenesis

Acne lesions have a problematic pathogenesis. The following are the 4 predominant mechanisms for the remedy of acne:

1. Enhanced sebum production;

2. Changed keratinization, leads to the comedones;

3. P. acnes migration to the follicle;

4. Inflammatory mediators are launched into the skin.

Acne can be exclusive by infection in the pilosebaceous unit. Plasmodium acnes is a key player in the pathogenesis of inflammatory acne.[15] .

P. acnes are a facultative anaerobe that is determined in the herbal plant life of the skin. In acne vulgaris, P. acnes stimulate innate immunity, inflicting each acute and persistent inflammation.[16] Oral anti-toxins have been acclimated with restriction the weight of P. acnes for pretty a while, however this doesn't imply that pores and skin damage out sores are cleared. Anti-toxins are utilized to treat skin spoil out due to their mitigating impacts, now not in view of their anti-microbial action.[17],[18],[19].

- Acne vulgaris therapy that is rational:

Acne vulgaris treatment can address a number of aspects of ailment pathogenesis at the equal time. It needs to listen on mixing goods with number ailment mechanisms in mind.[20]

Treatment effects are more advantageous when various marketers are used, each of which is structured on the moves of the others. Skin damage out ought to be dealt with as a constant condition, with treatment isolated into two stages: acceptance therapy to clear up most of sores, trailed by way of lengthy haul preventive treatment.[21]

- Topical agent:

Effective professionals are utilized by myself to treat gentle skin destroy out. For the enlistment and protection treatment of mild to outrageous pores and skin inflammation, it is utilized associated to oral therapies.[22]

1. Benzoyl peroxide (BPO) is an antibacterial substance. The drug has a high lipophilicity and is a effective oxidizer. It's keratolytic and anti-comedogenic, and it's extra bactericidal than topical antibiotics in opposition to P. acnes. BPO inhibits the development of Propionibacterium acnes barring inflicting bacterial resistance.[23]

During oral anti-microbial treatment, it improves the adequacy of oral anti-microbials and imitates the introduction of anti-toxin obstruction. The medicine has a strong safety profile, yet it can reason close by inconvenience from the start.[24] .

2. Retinoids are keratolytic, in opposition to comedogenic, and extremely calming superb retinoids. Effective retinoids help to oust enhance comedones and lessen the advancement of microcomedones.[25] Both comedonal and incendiary pores and skin inflammation respond well to these medicines. Skin retinoids are utilized as a first-line remedy for mild to serious pores and skin spoil out, just as for long haul upkeep.[26] It's no longer endorsed for the duration of being pregnant due to the fact it can purpose neighborhood irritation and photosensitivity, and it's no longer advocated for people with sensitive skin.[27]

3. Salicylic acid is a weakly keratolytic agent used in many over-the-counter preparations. Salicylic acid, however its decrease adequacy, is beneficial for patients who cannot suffer fine retinoids on account of skin disturbance.[28]

4. Azelaic acid has antimicrobial, keratolytic, mitigating, and cancer prevention agent properties.[29]

This professional decreases the association of comedones and can be utilized associated to one of kind medicines. It can likewise be utilized to treat post-inflammatory hyperpigmentation.[30]

5. Topical antibiotics are anti-inflammatory and act at once on P. acnes colonisation. When blended with BPO or a topical retinoid, these are established for mild to direct pores and skin inflammation. These have been linked to antibiotic resistance and need to not be used by them.[31] . [32] [33]

- Oral agents:

Oral isotretinoin is the fantastic skin damage out medicinal drug right now accessible. Since the medication raid every of the four of pores and skin inflammation's pathogenic pathways.[34] It's just utilized for outrageous nodulocystic pores and skin irritation or skin damage out that hasn't reacted to one-of-a-kind treatments because of its results.[35]

Dry skin, cheilitis, myalgias, photosensitivity, and abnormal liver ability tests with hyperlipidaemia are altogether everyday results. Since the medicine is a strong teratogen, girls must utilize exacting contraception. The first-rate component is 0.5–2.0 mg/kg/day, given greater than 4–6 months.[36] .

Anti-androgens are an adjunctive therapy for female pores and skin irritation patients. Seborrhea can be directed with oral contraceptives, cyproterone acetic acid derivation, and spironolactone (gluco-cortecoids).[37]

- Antibiotics for acne vulgaris (oral antibiotics):

Anti-microbials are utilized to treat skin spoil out due to their antibacterial and calming properties. Anti-infection treatment diminishes the extent of P. acnes microorganisms in the pilosebaceous unit whilst additionally stifling the host's incendiary response to the microscopic organisms.[38] [39]

These are for the remedy of fiery pores and skin ruin out that is gentle to genuine.[40]

At the point when skin drugs have fizzled, foundational anti-infection retailers can be utilized to assist with fiery skin inflammation.[41] . While making use of fantastic cure to a vast surface territory is beyond the realm of imagination, it may likewise be utilized for truncal skin destroy out.[42]

Antibiotic medications, macrolides, clindamycin, trimethoprim, cotrimoxazole, and quinolones are on the entire antimicrobials that have been regarded to neutralize P. acnes. Because of their greater calming properties, antibiotic medicinal drug anti-microbials are the most normally endorsed anti-infection agents.[43]

Antibiotic medicines are possibly the most typically utilized oral anti-toxins for pores and skin ruin out treatment.[44] .

These are lipophilic and work on the 30s ribosome subunits in nature, allowing medicinal drugs to go through the pilosebaceous unit.[45] .

Antibiotic medicinal drugs are anti-infection sellers that are utilized to deal with diseases of the respiratory lot. They can likewise be utilized to treat sufferers who are hypersensitive to penicillin.[46]

Antibiotic medications' non-antimicrobial residences have been efficaciously used to deal with non-irresistible dermatological conditions like rosacea.[47]

Antibiotic medications are mitigating capsules that reduce neutrophil chemotaxis and initiation, reduce incendiary cytokines, and prevent framework metalloproteinases, in addition to different things. Antibiotic medications have in opposition to oxidant and hostile to collagenolytic impacts also.[48] [49]

Doxycycline and minocycline are more recent generations of tetracyclines that are commonly used to treat acne. Minocycline has lengthy been favoured over other tetracycline antibiotics.[50] Minocycline use has declined in recent years, owing to the drug's high security profile. Minocycline has no definite advantage over other tetracyclines in phrases of efficacy or protection, according to a recent study. For the remedy of skin break out, doxycycline is presently the suggested first-line oral antibiotic medication.[51]

Queasiness, regurgitating, looseness of the bowels, oesophagitis, candidiasis, photosensitivity, photograph onycholysis, and favorable intracranial hypertension appearances are generally signs of antibiotic medications.[52]

In evaluation to minocycline, doxycycline is linked to gastrointestinal disturbance and photosensitivity. Minocycline is linked to a larger number of serious facet effects, some of which are permanent.[53]

Minocycline is the nearly all lipophilic antibiotic remedy anti-microbial that can cross the blood-cerebrum obstruction, inflicting vestibular results.[54]

It would possibly additionally end result in pores and skin discoloration that is blue-grey in colour. Minocycline-induced autoimmunity and doubtlessly deadly hypersensitivity reactions are uncommonly related with the drug.[55]

Tetracycline antibiotics are contraindicated all through being pregnant and breastfeeding because they can motive enamel discoloration and reduced bone growth.[56] .

Macrolides are bacteriostatic antibiotics that have anti-P. acnes recreation in vitro. In contrast to tetracyclines, macrolides have much less anti-inflammatory properties.[57] .

For patients who are unable to take tetracyclines, the use of macrolides ought to be restricted. Macrolides are secure to take for the duration of being pregnant and lactation.[58] Azithromycin has less gastrointestinal side effects than tetracyclines and is not linked to photosensitivity. Erythromycin resistance is every day in P. acnes. As a consequence, erythromycin usage for acne remedy has to be reduced.[59] [60]

- Antibiotic resistance linked to pimples remedy with oral antibiotics:

Anti-infection obstruction is a considerable universal well-being fear all in the course of the world. As a result, many people have a tendency to prescribe antibiotics rationally.[61] There is not lots proof that oral antibiotics are a protected choice for treating acne, and the size of remedy is additionally unknown. These doses are based totally on anecdotal proof alternatively than scientific proof.[62] . As a result, latest research have targeted extra on Dermatology and prescribing practises optimization. Skin infection is a non-irresistible pores and skin situation that is dealt with with anti-microbials in reality for their mitigating properties.[63] Acne is dealt with with antibiotic regimens that encompass the use of low-dose antibiotics on a ordinary basis. This squeezes the microscopic organisms, enabling anti-toxin protected lines to advance.[64] . Topical antibiotics purpose is

resistance to boost only on the skin of the dealt with areas. Skin ailments precipitated via the Propionibacterium micro organism are resistant to antibiotics.[65]

Anti-microbials have been utilized to deal with skin spoil out for extra than forty years. Furthermore, an increment in the commonness of anti-infection secure P. acnes traces has been seen in the path of the most current twenty years.[66] mechanisms include factor mutations in genes that code for ribonucleic acid.[67]

- Hormonal Therapy

Hormonal therapy is truly used to treat pores and skin irritation in ladies. These medicines, which restrict androgen articulation, are headquartered on the part of androgens in the pathophysiology of pores and skin irritation advancement.[68] Oral contraceptives (OCs) and androgen-receptor blockers such as flutamide, spironolactone, and cyprone acetic acid derivation are cases of antiandrogenic compounds.[69] .

Various oral contraceptives have as of late been licensed for use in the remedy of skin spoil out. Oral contraceptives limit bioavailable testosterone and put off ovarian androgens with the aid of an estrogen-mediated mechanism that will increase the steroidal hormones that connect to globulin.[70]

Progestin and cyproterone are succesful androgen-receptor blockers that cause prostate most cancers in guys and acne, hirsutism, and polycystic ovary syndrome in ladies when administered in greater doses.[71]

Flutamide is a non-steroidal androgen receptor blocker that is utilized to deal with skin irritation and hirsutism in female.[72]

- Retin-A (Isotretinoin)

Isotretinoin is a nutrient A metabolite that stifles sebum arrangement, decreases sebaceous organ size, and standardizes follicular epithelial desquamation by using hindering sebaceous organ separation and expansion.[73]

It is utilized at a portion of 0.5 to 1 mg/kg each day with blended measurements of 120 to 150 mg/kg over a 4 to 1/2 year cure range, in excessive nodular zits and zits that has now not answered to other therapies.[74] Dry eyes, dry lips, dry face, backapin, reduced night time vision, and epistaxis are all facet results of isotretinoin. Bilateral intracranial hypertension is a less common side effect. Isotretinoin has been linked to a gentle to direct enlargement in liver proteins simply as serum lipid lists, in particular fatty oils.[75]

- Mild to Moderate Severity Inflammatory Acne

There are a few choices, which include benzoyl peroxide, azelaic corrosive, clindamycin, erythromycin, and double specialists containing benzoyl peroxide and either erythromycin or clindamycin.[76].

Effective antimicrobials can be utilized related to fantastic retinoids, as per present proposals. 2-Benzoyl peroxide is a modest and proficient antimicrobial that is not recognized with antimicrobial obstruction when utilized at fixations going from two to 20%.[77].

Anti-toxins on my own are ineffectual contrasted with double expert gadgets that be a part of tremendous anti-microbials (clindamycin, erythromycin) and benzoyl peroxide.[78]

- Moderate to Severe Inflammatory Acne

The primary line remedy is oral antibiotics such as tetracyclines (minocycline, doxycycline, and tetracycline). Erythromycin is recommended.[79]

It is used much less frequently because of its relation to P acnes that are antibiotic-resistant. In spite of the truth that, trimethoprim sulfamethoxizole has been demonstrated to be fruitful the chance of intense results is inadmissibly high.[80]

- Severe Papulonodular Acne

Outrageous papulonodular acne, therapy disappointments, scarring, and persistent skin smash out, simply as situations of true mental trouble, are treated with oral isotretinoin.[81]

Isotretinoin is utilized as a solitary remedy treatment, except for women for whom associative Oral contraceptives are energetically suggested.[82]

Day by way of day portions of 1 mg/kg every day for span of 20 weeks provide the pleasant results or a complete collective element of 120 mg/kg.[83]

Broad erosive sores, fever, arthralgias, and leukocytosis are for the most phase warning signs of pores and skin wreck out fulminans, a abnormal isotretinoin result. Treatment with integral corticosteroids is required. Prednisone at 0.5 to 1.0 mg/kg each day for 4 to about a month and a half of gives you the first-class outcomes, with isotretinoin persisted on week four at 0.5 mg/kg each day and persistently expanded.[84]

- Women with pimples

Hormone imbalances have been handled with oral contraceptives or androgen-receptor blockers. It has been validated to be invaluable. For a woman with acne out who wishes to make use of anti-conception medication, oral contraceptives are the most secure alternative.[85] Oral contraceptives are now not an exception; popular therapies are needed. Oral contraceptives licenced for zits care include Orthotricyclin, Estrostep, and Diane-35. Androgen-receptor blockers, both by ownself or in aggregate with oral contraceptives, have a response charge of fifty to eighty percentages for those who do no longer reply to oral contraceptives.[86]

Flutamide at 250 mg/d is some other well-tolerated treatment.[87]

Hepatotoxicity and gastrointestinal upset are additionally manageable facet results at greater dosages. Intermittent liver ability tests are cautioned for all flutamide measurements.[88]

➢ Antioxidant Properties of Flavonoids

The antioxidant properties of flavonoids are usually claimed to be in charge for the protective results of these compounds in opposition to cardiovascular disease, certain types of cancer, photosensitivity diseases, and inflammations. They can additionally inhibit a wide range of enzymes worried in oxidation reactions, such as 5-lipoxygenase, cyclooxygenase, monooxygenase, or xanthine oxidase. These natural things to do include the formation of reactive-oxygen suppressing species, both by using inhibition of enzymes or via chelating trace elements concerned in free-radical production, scavenging reactive species, and regulating or defending antioxidant defenses. At least two mechanisms concerned in the antioxidant strategies are known: a direct hydrogen atom change process or an electron transfer process. So this undertaking depends in general on the substitution pattern of the hydroxyl groups, that is to say, on the availability of phenolic hydrogens and on the possibility of stabilizing the resulting flavonoid phenoxyl radicals.The figure below mentioned offers the general structure of flavonoids, our ring notation and our atom numbering. The structural necessities considered essential for superb radical scavenging by flavonoids are the presence of 3', 4'-dihydroxy group (catechol) in the B ring and/or the presence of the 3-OH crew in the C ring. In addition, the 5- OH crew in aggregate with a 4-oxo moiety (1, 4-pyrone moiety) and C2=C3 double bond might also amplify the radical scavenging endeavor. Numerous authors have investigated the antioxidant activity of flavonoids, and many tries have been made to establish the relationship between flavonoid structure and their radical scavenging endeavor.

CHAPTER 4. SURVEY

1. Gender
    - Male
    - Female
    - Other:

2. The age category you belong to
    - 18-25 years
    - 26-35 years
    - 36-45 years
    - More than 46

3. What do you prefer for Acne treatment?
    - Home remedies
    - Cosmetics

4. Which of these cause acne?
    - Not keeping skin clean
    - Not eating healthy diet
    - Not getting exercise
    - None of these

5. Where does acne most often show up!

- Face
- Back
- Shoulder
- All of the above

6. Acne can be treated with which of these?

- Skin cleanser
- Oral antibiotic
- Oral vitamin and medicine
- All of these

7. How does being in Sun affect acne?

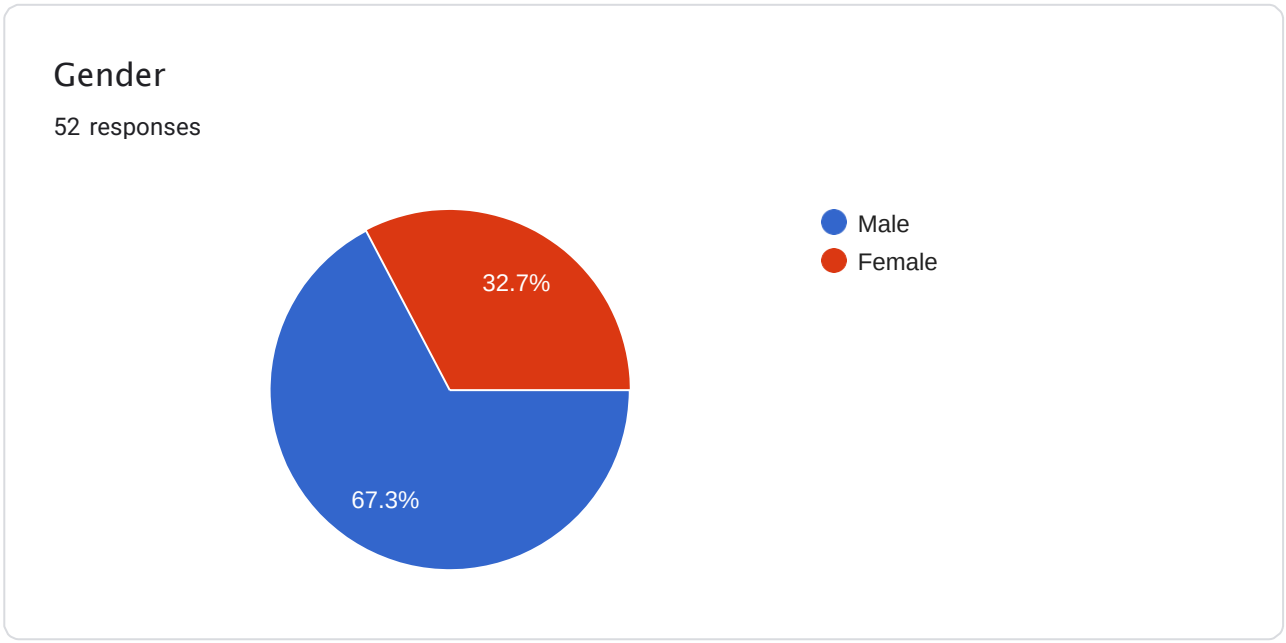
- Clear a pimple
- Boost the amount of oil skin makes
- Makes scars less visible
- All of the above

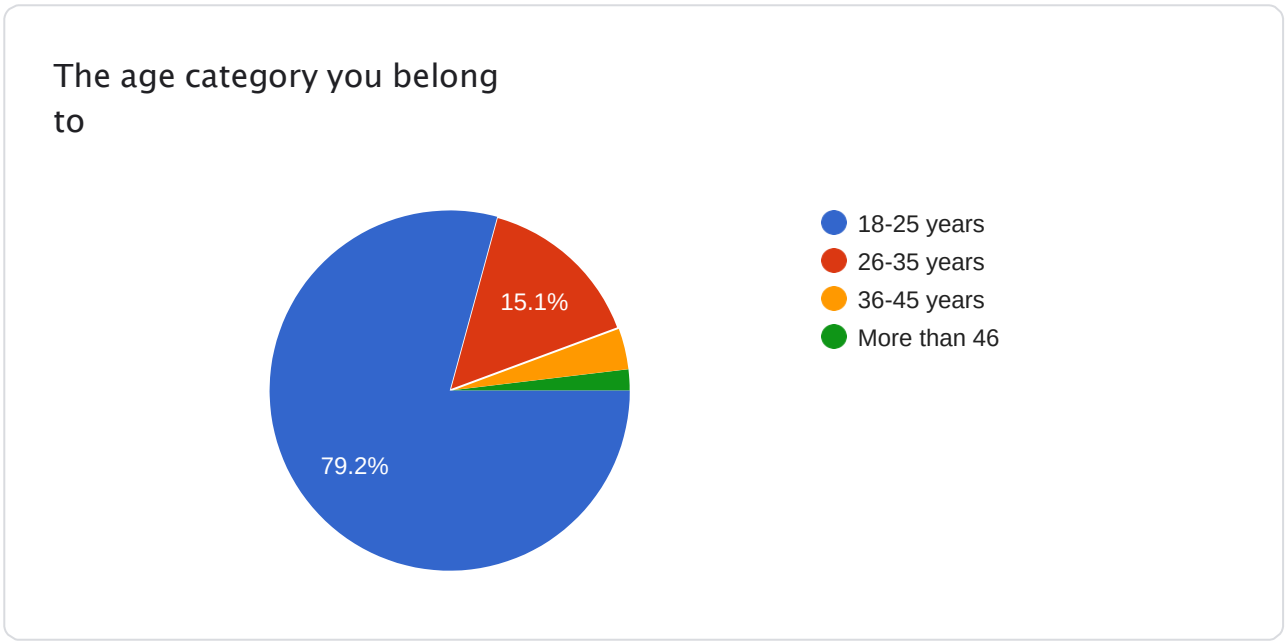
8. What Lifestyle factor contributes to human acne?

- Smoking
- Drinking
- Diet
- All of the above

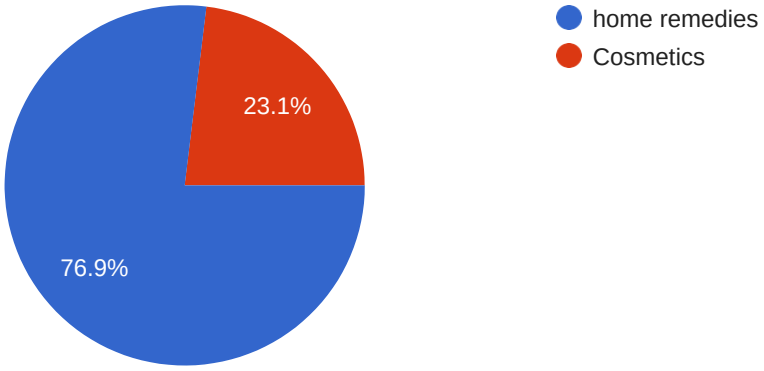
9. What is the Best acne treatment?

Any suggestions…..

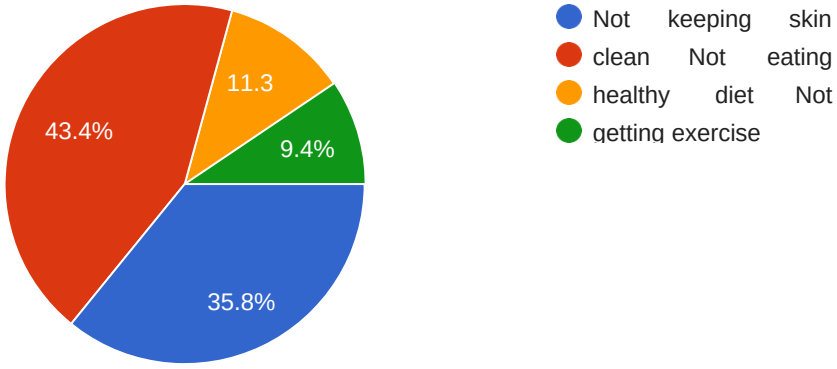




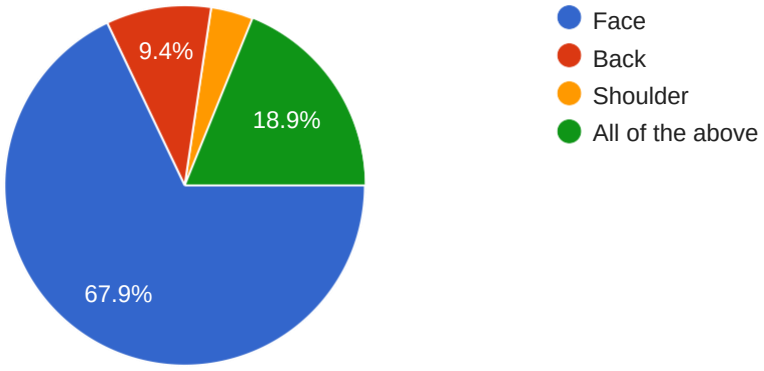
What do you prefer for Acne treatment?



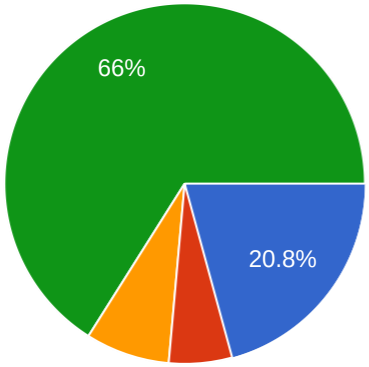
Which of these cause acne?



Where does acne most often show up!

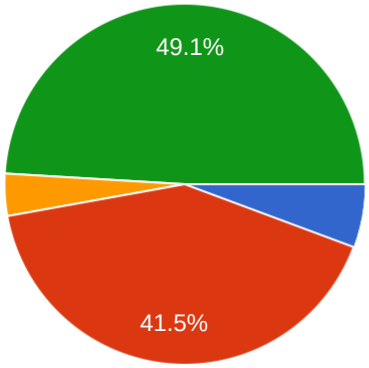


Acne can be treated with which of these?



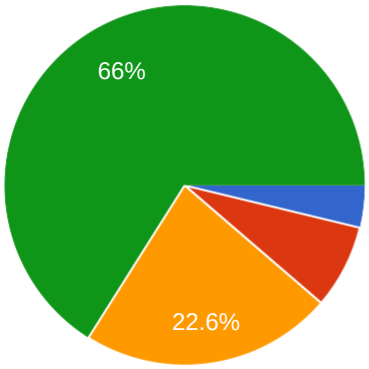
- Skin cleanser
- Oral antibiotic
- Oral vitamin and medicine
- All of these

How does being in Sun affect acne?



- Clear a pimple
- Boost the amount of oil skin makes
- Makes scars less visible
- All of the above

What Lifestyle factor contributes to human acne?



- Smoking
- Drinking
- Diet
- All of the above

What is the Best acne treatment? Any suggestion

I don’t know much about that

Apply sandalwood powder with rose water

Have lots of water!

Proper medical treatment

Turmeric and lemon

No i dont know

Sandal wood powder with rose water.

Wash your face thoroughly.

No

AutoDock Vina employ for Docking protein JNK1 (1UKI PDB) inhibition of action associated in Acne.

JNK, c-Jun N-Terminal Kinase also known as stress-activated protein kinases(SAPK), it represent the subfamily of canonical MAPK signaling transduction pathway.[102] It consist the various proteins like JNK1,JNK2 and JNK3 which encoded by the separated genes such as Mapk8, Mapk9, and Mapk10, respectively.[103] JNK proteins are highly responsible in various array of cellular stimuli, including inflammatory cytokines, growth factors, UV radiation, bacterial and viral infections, heat shock, and osmotic and genotoxic stresses.[104-107]

Acne is a skin condition caused by oil and dead skin cells clogging our hair follicles. Blackheads, whiteheads, and pimples are all caused by acne. It usually begins with enlarged facial grease development and mid-facial comedones, accompanied by inflammatory lesions, in early puberty.[1]

Excess oil (sebum production), clogged hair follicles with oil and dead skin cells, bacterial infection, and inflammation are the four major factors that cause acne.[2]

Autodock vina performance

AutoDock Vina performed over the selective compound *SP600125,* ternary complex structure with JNK1 protein makes two hydrogen bonds with Met111 and Glu 109 amino acids associated commonly in many structure to inhibitor-bound kinase and other than *SP6000125*, makes interaction hydrophobic residues in adenine-binding pocket of protein molecule such as Ile32, Val40, Ala 53, Ile86, Met108, Leu110, Val158, and Leu168 with effective van der Waals contact in JNK specificity complex with this compound.[108]

We demonstrate docking with this same selective compound *SP600125* with performing all procedure via using AutoDock vina and make possibilities of compound enlist associated to overcome or prevent the action of inflammation associated JNK1 selective in Acne.

Preparation of ligand and macromolecule

1. Collection of compounds from PubChem database[109]

Collection of compounds from PucbChem includes are 9-(Pyridin-2-ylmethyl)acridine(PubChem CID –41872); 2,4,6,8-Nonatetraenoic acid, 9-(3-chloro-2,4,6 -trimethylphenyl)-3,7-dimethyl-, ethyl ester, (all-E)-(PubChem CID – 6443432); 9-(4-methoxy-2,3,6-trimethylphenyl)-3,7- dime thylnona- 2,4,6,8-tetraenoic acid ethyl ester (PubChem CID –3312); Retinoid(PubChem CID 5282375); 9-(2,3,6-trichloro-4-methoxyphenyl)-3,7-dimethyl nona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID –204051); (2E,4E,6E,8E)-9-(2,3,6-Trichloro-4-methoxyphenyl)- 3,7-

dimethyl-2,4,6,8-nonatetraenoic acid ethyl ester (PubChem CID – 6507142); 9-(2,6-Dichloro-4-methoxy-5-methyl-phenyl)-3,7-dimethyl-nona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID – 127591); 2-Hydroxyquinoline (PubChem CID –6038); Salicylic acid (PubChem CID – 338) and Azelaic acid (PubChemCID – 2266).

2. Preparation drug molecule and protein structure

Drug molecule prepare by the following steps are includes such as ligand convert into 3D struc ture with explicit Hydrogen and optimized with energy to reduce the torsion and make flexible with different model of structure generation.

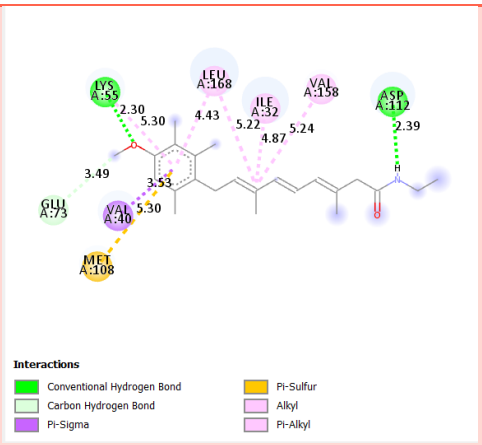
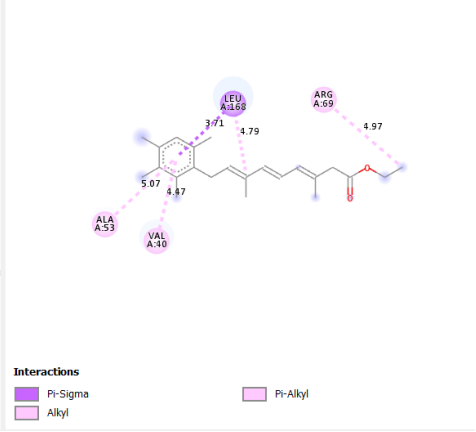
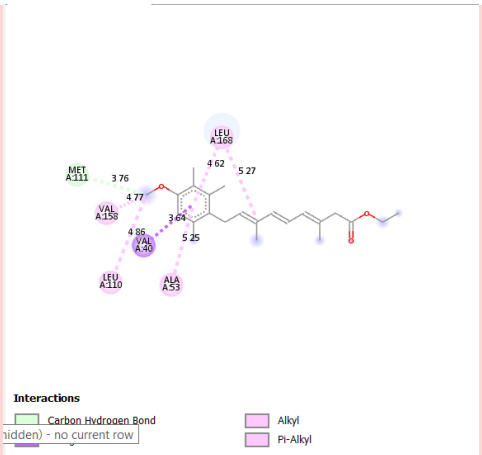
Protein molecule preparation via using ADT tool[110] with optimized all parameters with target se lective chain and amino acids in given protein molecule and further performed the AutoDock Vina to final complex result of docking.

. AutoDock Vina results enlisted with energy level of score

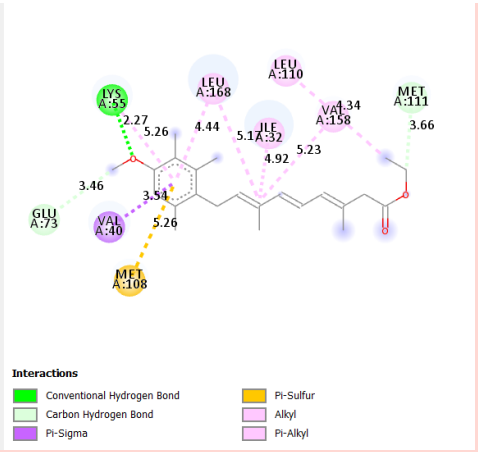
LIGANDS	RMSD VALUE (Kcal/mol)
1. 9-(Pyridin-2-ylmethyl)acridine (PubChem CID – 41872)	-8.0
2. 2,4,6,8-Nonatetraenoic acid, 9-(3-chloro-2,4,6 trimethylphenyl)-3,7-dimethyl-, ethyl ester, (all-E)- (PubChem CID – 6443432)	-7.9
3. 9-(4-methoxy-2,3,6-trimethylphenyl)-3,7-dimethylnona- 2,4,6,8-tetraenoic acid ethyl ester (PubChem CID –3312)	-7.7
4. Retinoid (PubChem CID –5282375)	-7.7
5. 9-(2,3,6-trichloro-4-methoxyphenyl)-3,7-dimethyl nona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID – 204051)	-7.3
6. (2E,4E,6E,8E)-9-(2,3,6-Trichloro-4-methoxyphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid ethyl ester (PubChem CID – 6507142)	-7.3
7. 9-(2,6-Dichloro-4-methoxy-5-methyl-phenyl)-3,7-dimethyl-nona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID – 127591)	-7.1
8. 2-Hydroxyquinoline (PubChem CID – 6038)	-6.1
9. Salicylic acid (PubChem CID – 338)	-5.2
10. Azelaic acid (PubChem CID – 2266)	-5.1

POST DOCKING ANALYSIS

Visualization of Docking results via using Discovery Studio Visualizer 2020 (DassaultsystèmesBioviacorp)[111] and predict the best approaches compounds list on the basis of score and binding interaction.

NAME OF LIGANDS	DOCKING VISULIZATION	LOG FILES
1. 9-(Pyridin-2-ylmethyl)acridine (PubChem CID – 41872)		mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b. -----+----------+---------+--------- 1 -8.0 0.000 0.000 2 -7.8 1.580 1.697 3 -7.8 0.738 2.000 4 -7.5 1.726 2.415 5 -7.3 2.773 3.692 6 -7.3 1.615 2.676 7 -7.3 4.283 11.259 8 -7.3 6.024 12.430 9 -7.0 6.040 12.482 Writing output ... done.
2. 2,4,6,8-Nonatetraenoic acid, 9-(3-chloro-2,4,6 trimethylphenyl)-3,7-dimethyl-, ethyl ester, (all-E)- (PubChem CID – 6443432)		**mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b.** **-----+----------+---------+---------** **1 -7.9 0.000 0.000** **2 -7.7 1.426 2.225** **3 -7.4 7.038 11.015** **4 -7.4 7.275 12.824** **5 -7.3 7.395 12.502** **6 -7.1 7.185 12.011** **7 -7.0 7.260 11.744** **8 -6.9 7.291 12.499** **9 -6.9 7.808 12.298** **Writing output ... done.**
3. 9-(4-methoxy-2,3,6-trimethylphenyl)-3,7- dimethylnona-2,4,6,8-tetraenoic acid ethyl ester (PubChem CID – 3312)		mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b. -----+----------+---------+--------- 1 -7.7 0.000 0.000 2 -7.6 4.581 12.471 3 -7.5 0.968 2.319 4 -7.5 4.721 12.319 5 -7.4 4.322 12.287 6 -7.1 1.592 2.753 7 -7.1 1.226 2.550 8 -7.1 1.476 2.176 9 -7.0 4.885 12.144 Writing output ... done.

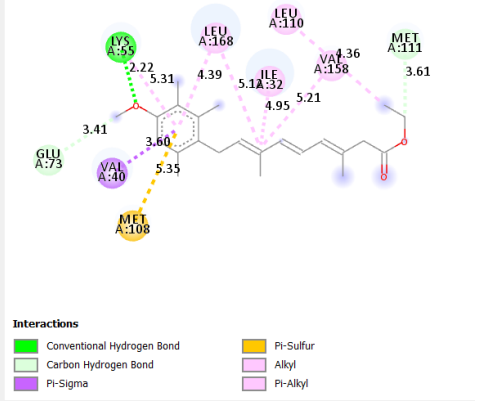
4. Retinoid (PubChem CID – 5282375))



mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-7.7	0.000	0.000
2	-7.6	4.597	12.420
3	-7.6	4.419	12.242
4	-7.6	4.565	12.169
5	-7.5	0.939	1.751
6	-7.4	0.738	2.009
7	-7.1	1.506	2.998
8	-6.8	3.212	4.883
9	-6.7	2.872	4.565

Writing output ... done.

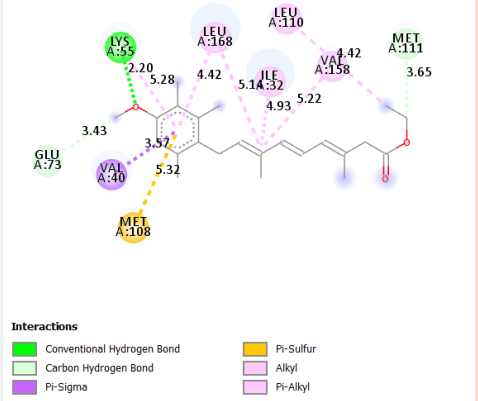
5. 9-(2,3,6-trichloro-4-methoxyphenyl)-3,7-dimethylnona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID – 204051)



mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-7.3	0.000	0.000
2	-7.1	4.686	12.293
3	-7.0	1.166	2.178
4	-7.0	1.223	1.678
5	-6.8	1.286	2.509
6	-6.8	4.867	11.603
7	-6.6	4.826	12.222
8	-6.6	1.783	3.104
9	-6.4	3.222	4.891

Writing output ... done.

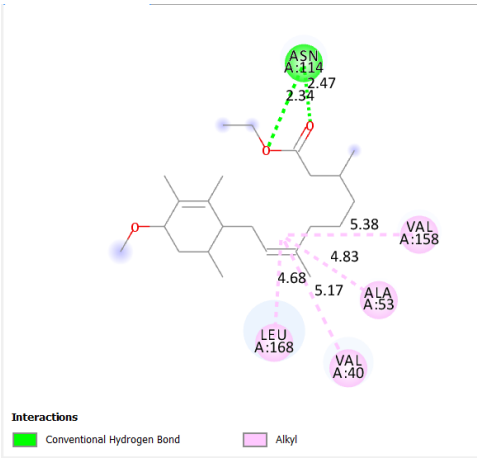
6. (2E,4E,6E,8E)-9-(2,3,6-Trichloro-4-methoxyphenyl)-3,7-dimethyl-2,4,6,8-nonatetraenoic acid ethyl ester (PubChem CID – 6507142)



mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-7.3	0.000	0.000
2	-7.0	4.479	12.463
3	-6.9	4.903	11.970
4	-6.9	1.597	2.481
5	-6.8	1.557	2.875
6	-6.8	2.982	4.328
7	-6.8	4.852	11.999
8	-6.4	1.946	3.090
9	-6.3	5.593	11.899

Writing output ... done.

7.
9-(2,6-Dichloro-4-methoxy-5-methyl-phenyl)-3,7- dimethyl-nona-2,4,6,8-tetraen-1-oic acid ethyl ester (PubChem CID – 127591)

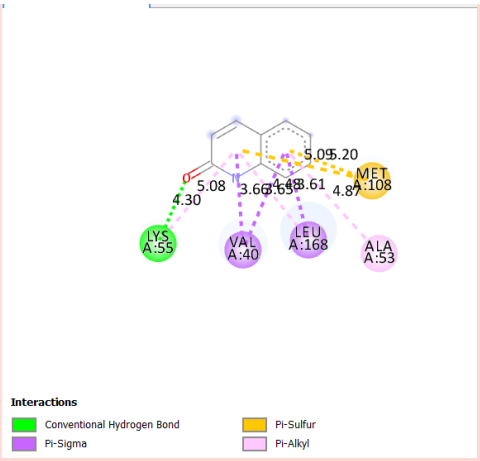


mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b.

1	-7.1	0.000	0.000
2	-6.7	2.119	6.762
3	-6.6	1.581	2.460
4	-6.6	2.128	6.747
5	-6.4	1.986	6.480
6	-6.3	1.793	2.206
7	-6.3	2.006	3.965
8	-6.2	1.447	2.528
9	-6.1	2.802	7.827

Writing output ... done.

8.
2-Hydroxyquinoline (pubchem CID – 6038)

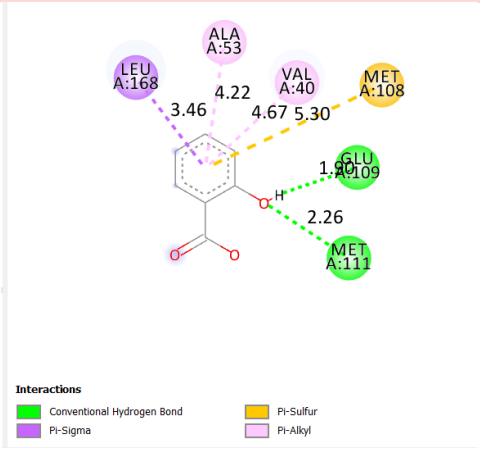


mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b.

1	-6.1	0.000	0.000
2	-5.9	1.334	2.194
3	-5.8	3.675	5.408
4	-5.8	2.070	3.443
5	-5.7	2.573	4.451
6	-5.6	1.447	2.427
7	-5.6	2.170	3.526
8	-5.6	1.504	1.927
9	-5.5	4.907	6.156

Writing output ... done.

9.
Salicylic acid (pubchem CID – 338)

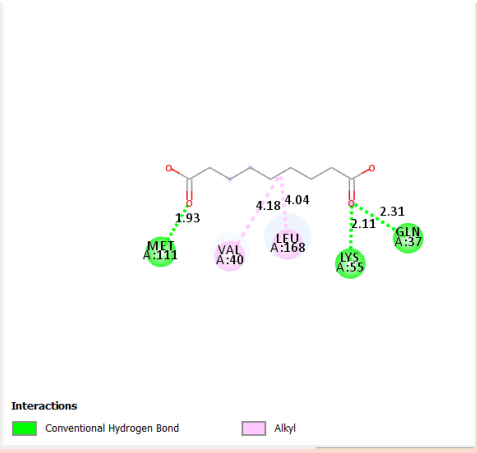


mode | affinity | dist from best mode | (kcal/mol) | rmsd l.b.| rmsd u.b.

1	-5.2	0.000	0.000
2	-5.2	0.933	2.429
3	-5.2	1.204	2.036
4	-5.0	5.700	6.748
5	-5.0	1.201	3.166
6	-4.8	4.732	6.128
7	-4.7	4.389	5.356
8	-4.6	2.059	3.405
9	-4.6	6.949	7.904

Writing output ... done.

10.
Azelaic acid (pubchem CID – 2266)



mode	affinity (kcal/mol)	dist from best mode rmsd l.b.	rmsd u.b.
1	-5.1	0.000	0.000
2	-5.0	1.187	6.944
3	-5.0	1.739	7.182
4	-4.9	4.631	5.979
5	-4.6	2.321	7.171
6	-4.6	2.262	3.274
7	-4.5	3.701	7.272
8	-4.5	5.029	6.682
9	-4.5	3.116	7.131

Writing output ... done.

Conclusion:

Acne is persistent in nature however there high-quality treatments on hand in the society. Even after healing of pimples it leaves black spots and scar on the pores and skin which reasons intellectual stress finally there are positive beauty available that eliminates the scar precipitated by way of acne. The 4 primary mechanisms which are carried out within the remedy of acne:

1. Enhanced sebum production;

2. Changed keratinization, leads to the comedones;

3. P. acnes migration to the follicle;

4. Inflammatory mediators are released into the skin.

Oral anti-microbials have been utilized for quite a while to minimize the strain of P. acnes, then again this doesn't infer that pores and skin wreck out sores are cleared. Anti-toxins are utilized to deal with skin ruin out due to their mitigating impacts, not on the grounds that they are anti-microbials. Gentle pores and skin irritation would possibly be treated with simply an fantastic specialist. It's utilized related to oral skin spoil out treatment plans such as Benzoylperoxide, Retinoids, Salicylic corrosive, Azelaic corrosive, and pores and skin anti-toxins for enlistment and assist cure of gentle to outrageous skin inflammation.

Oral isotretinoin is the exceptional pores and skin irritation medicine accessible, in view that it tends to each of the 4 pores and skin irritation pathogenic pathways.

1. Anti-androgens are utilized as an adjunctive therapy for female skin break out patients. Seborrhea can be managed with oral contraceptives, cyproterone acetic acid derivation, and spironolactone (gluco-cortecoids).

2. Antibiotics are utilized to deal with skin break out in mild of the fact that they are both antibacterial and calming. Anti-microbial treatment diminishes the volume of P. acnes microbes in the pilosebaceous unit while moreover smothering the host's incendiary response to the microscopic organisms. These are for the therapy of fiery pores and skin damage out that is mild to extreme. Tetracycline, doxycycline, macrolie, and azithromycin are cases of foundational anti-toxins that might be utilized to treat provocative skin damage out when pores and skin drugs have fizzled.

Oral anti-microbials, especially antibiotic medications, have calming homes that help to treat incendiary pores and skin break out. Anti-biotic used for pores and skin damage out reasons obstruction in P. acnes, simply as one of kind microbes in the host. Anti-microbial stewardship ought to be a first difficulty for dermatologists to forestall anti-microbial opposition because of pores and skin infection care. Oral anti-infection sellers should be utilized for enlistment cure and for a quick timeframe. Anti-toxins ought not to be utilized for significant stretches of time in mild of the fact that one-of-a-kind experts of similar adequacy are on hand for aid treatment. Both anti-microbial guides ought to be joined by a wonderful non-anti-microbial specialist, for example, an

advantageous retinoid or BPO. Doxycycline at a sub antimicrobial component ought to be concentrated further. Effective daps one can deal with skin wreck out irritation whilst preserving away from the development of anti-infection opposition.

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