Field of Research	**Pharmacy**
Level of Study	PhD
Research Topic	Formulation and Characterization of Polyherbal Phytosomal gel for Tinea infection

1.0 Introduction&Literature review

Tinea is a skin disease that begins as erythematous scaly papules and develops into annular or nummular red patches or plaques, often with a clearing in the centre and surrounding scales. Tinea refers to a fungal infection caused by dermatophytes such as tineacorporis or tineapedis that affect hair, nails, and the stratum corneum that are immune to other pathogens. Tineacorporis and tineacapitis are the most common infections in children before puberty, while tineacruris, tineapedis, and tineaunguium are more common in adolescents and adults (onychomycosis). Lesions may be solitary or numerous and vary in size from 1 to 5 cm, although larger lesions and the coincidence of lesions are also possible.
Fungal infections are on the rise, causing high rates of morbidity and mortality worldwide. The prevalence of increasing treatment resistance in fungal infections and the emergence of new fungal species is increasing. The current status of antifungal drugs and their side effects are of great concern. Decreased fungistatic activity, severe toxicity, and renal failure are all disadvantages of antifungal drugs. Therefore, it is crucial to search for new drugs that could be effective as alternative treatments against most fungal infections. Flavonoids are found in medicinal plants and are known to be safe and have a variety of biological activities. Several flavonoids have been isolated and studied for their antifungal properties, and they could be promising, efficient, and cost-effective drugs for the prevention of fungal infections. By enhancing plasma membrane rupture and mitochondrial dysfunction, and suppressing cell wall assembly, cell division, protein synthesis, and efflux-mediated pumping system, they often limit fungal growth. These flavonoids are competent and effective in synergistic combination therapy with conventional drugs, which may be more suitable and conducive for the development of new antifungal agents. Recently, it has been shown that the phospholipid complex technique can eliminate these stumbling blocks, i.e., phytocomponents, by either increasing their solubility or enhancing their ability to penetrate biological membranes and protecting the active plant constituents from degradation. As a result, researchers will be able to readily transport phytoconstituents into the bloodstream using this phospholipid complex method. Therefore, the goal of this study is to develop a polypharmaceutical formulation that more effectively transports active ingredients for the treatment of tinea infections. The formulation produced would allow for regulated drug delivery into the deep layers of the skin, improving drug bioavailability and stability while increasing patient compliance.

HarisunYaakob et al., (2020) The Bioassay-Guided Different Extraction Techniques of *Carica papaya* (Linn.) Leaves on in Vitro Wound-Healing Activities. The present study aims to investigate the effects of three different non-conventional extraction techniques (ultrasonic-assistedextraction,reflux,andagitation)on*Caricapapaya*phytochemicalconstituents,theantioxidant capacity,andwound-healingactivities.Amongthethreetechniques,therefluxtechniqueproduced the highest extraction yield (17.86%) with the presence of saponins, flavonoids, coumarins, alkaloids,andphenolicmetabolites.Therefluxtechniquealsoproducedthehighest2,2-diphenyl- 1-picrylhydrazyl (DPPH) radical scavenging with an IC50 value of 0.236 mg/mL followed by ultrasonic-assistedextraction(UAE)(IC50:0.377mg/mL)andagitation(IC50:0.404mg/mL).At testedconcentrations(3.125µg/mLto500µg/mL),allextractsdonotexhibitorytotoxicityeffect on the human skin fibroblast, HSF1184. Interestingly, reflux and UAE were active fibroblast proliferators that support 85% (12.5 µg/mL) and 41% (6.25 µg/mL) better cell growth, respectively.

Skaltsa Helenetal.,(2020) Investigatedthepotentialbeneficialeffectsinpsoriasisinmiceof M. officinalis ssp.altissimaandtocarryoutthechemicalanalysisinrertorevealitsmainbioactive secondary metabolites. Non polar and polar extracts of M. officinalis ssp. altissima aerial parts were prepared by using dichloromethane and methanol, successively; in addition a decoction was made upon oral information by local users in Crete, where the plant was collected. All three preparations were chemically analyzed in order to isolate their main constituents. Chemical structuresofallisolatedcompoundsweredeterminedby1D,2D-NMRandUV–Visspectroscopy.
Furthermore, the antioxidant potential of extracts and decoction was evaluated through DPPH radical scavenging capability. The in-vivo in mice anti-psoriatic efficacy of all preparations was estimatedthroughclinicalandhispathologicalassessmentandmeasurementsofTEWLand hydration. The dichloromethane extract yielded ursolic acid, 2α-hydroxy-ursolic acid, pomolic acid, 3β stearyloxyurs-12-ene, oleanolic acid, noropacursane and campesterol; the methanol extract afforded rosmarinic acid and methyl rosmarinate,whilefromthedecoctioncaffeicacid,3- (3,4-dihydroxyphenyl)lactic acid and rosmarinic acid were isolated. The psoriasis evaluation, based on PASI score, photodocumentation and histopathological estimation showed that the decoction primarily and the dichloromethane extract secondly could significantly contribute to psoriasistreatment.

You Fang et al., (2019) The development of an apoptotic or anti proliferative strategy for natural-product management in the treatment of psoriasis. Systematically introduce the concepts and molecular mechanisms of keratinocyte-proliferation inhibition by crude extracts or natural compounds that were isolated from natural resources, especially plants. Most of these studies focus on evaluation through an in vitro keratinocyte model and an in vivo psoriasis-like animal model. Topical delivery is the major route for the in vivo or clinical administration of these natural products. The potential use of antiproliferative phytomedicine on hyperproliferative keratinocytessuggestsawayforwardforgeneratingadvancesinthefieldofpsoriasistherapy.

Muhammad Daniyal et al., (2019) Reviewed the efficacy of herbal and allopathic drugs used to manage and treat psoriasis. Psoriasis is a common skin disease affecting 2–3% of the world's population. It is cosmetically debilitating and chronic disease, which occurs both in developing and developed countries. It can affect any part of the body, but the most common sites are the elbows, knees, and scalp. It is usually treated with synthetic medicine either given systematically or applied locally. The prescribed synthetic medicines used for the treatment of psoriasis are associated with severe side effects and complications, thus researchers around the world are trying to explore new, more effective, and safer drugs from natural resources. Medicinal plants are safe and efficacious and most of the people all over the world rely on herbal medicine due to the easy availability, low cost, and efficacy for treating psoriasis. A number of medicinal plants having therapeutic potential with high efficacy are used in the treatment of psoriasis have been described. Moreover, studies should be conducted to isolate and investigate the mechanism of actions of phytochemicals responsible for anti-psoriasispotential

Literature Review on formulation design and delivery-Technology

Molaveisi M. et al., (2021) Encapsulated Resveratrol (RES), a well-known bioactive compound within nano-phytosome (RES-PHY) for application in mayonnaise. The physico-chemical, microstructure, physical stability, antioxidant activity, encapsulation efficiency (EE%) were

evaluated. The particle size, polydispersity index (PDI), and zeta-potential (ζ) of the RES-PHY-nanoparticles were recorded by dynamic light scattering (DLS) as 78.7 nm, ~0.18, −15.9 mv and spherical shapes of the particles with the size under 100 nm were proved by scanning electron microscopy (SEM). The High-Performance-Liquid-Chromatography (HPLC) indicated the EE of 85%. Fourier-transform infrared spectroscopy (FTIR) and X-ray diffraction (XRD) analyses showed the well-insertion and homogenous embedment to fRES with inPHY-Nano carrier according to the formation of new hydrogen bonds and amorphous structure of RES-PHY. During 60 days storage of RES-PHY-solution, the particles remained at ~112 nm with a unimodal distribution. The antioxidant activities of RES-PYH-enriched mayonnaise were respectively 84, 82, and 81% after 14, 30, and 60 days of storage that were higher than control samples with pure-RES (75, 62, and60%)and citric acid (82, 80, and79%). to maintain the antioxidant properties of RES in mayonnaise during shelf-life and could be considered in high-fat foods to reduce oxidation and enhance their nutritional properties.[93] Improved the oral bioavailability by formulating *Echinacea* extract (EE) phytosome developed for oral consumption. *Echinacea* extract phospholipid phytosome (EPLP) was optimized by applying a simple centroid mixture design with particle size, encapsulation yield, and the release of bioactive compounds in the simulated digestion media as response factors. Optimized EPLP was then added to an acidic food beverage and evaluated for stability, antioxidant activity, sensory properties, and *in vitro* release. Complexation of EE with phospholipids increased the stability and antioxidant activity of its bioactive compounds in the acidic food beverage for up to 30 days of storage. Furthermore, formulation as EPLP resulted in mask the poor taste of EE. The results indicate the potential of nano phytosomes to improve oral bioavailability of EE by increase the stability of its bioactive compounds in the acidic food beverage.

Ebada Heba M.K et al., (2021) elaborated RH loaded trans phytosome (RH-T-PHY) as novel nano vesicular systems for transdermal drug delivery based on an advantageous hybrid between phytosomes and transfersomes or bilosomes. Here, we developed transphytosomes through incorporating various edge activators (EAs) such as Tween 80, Span 80 and sodium deoxycholate into the lipid bilayer of RH phytosomes to affix the flexibility. RH-T-PHY with high flexibility and entrapment efficacy showed the highest significant skin permeation compared to conventional phytosomes. Additionally, RH-T-PHY have a magnificent potential in maintaining high chondro protective activity as demonstrated by enhanced repair, regeneration of chondrocytes and GAG formation in MIA-induced osteoarthritis (OA) rat model. Besides, histological examination of vital organs revealed the formulation safety. Confocal laser microscopy images revealed the highest drug availability in the articular cartilage of RH-T-PHY treated group. Conclusively, novel RH-T-PHY canserve as a promising alternative means for delivery of chondro protective drugs for effective non-invasive local therapy of OA.

Zhu S et al., (2020) developed nano medicine containing Tri and Se used for fighting against arthritis via a coordination mechanism.Se-deposited Tri phytosomes (Se@Tri-PTs)were prepared by a melting-hydration/*in situ* reduction technique and characterized by particle size, ζ potential, morphology, and entrapment efficiency(*EE*).The resultantSe@Tri-PTswere126 nm around in particle size with an *EE* of 98.85%. Se@Tri-PTs exhibited a sustained drug release both in 0.1 M HCl and pH 6.8 PBS compared with Se-free phytosomes (Tri-PTs). The *in vivo* anti-arthritic test demonstrated that Se@Tri-PTs could result in significant resolution of arthritis and decline of inflammatory factors. Phytosomes primly facilitated the trans epithelial transport of Tri, while Se

enhanced the antiarthritic efficacy of the phyto medicine synergistically. The present work provides a proof-of-concept for the combined therapy of arthritis using Tri and Se in the form of nanoparticles.

Literature Review on a few antifungal drugs

Literature Review based on Silymarin

Delmas D et al., (2020) summarized the current knowledge on the potential targets of silymarin against various cancers. Silymarin may play on the system of xenobiotics, metabolizing enzymes (phase I and phase II) to protect normal cells against various toxic molecules or to protect against deleterious effects of chemotherapeutic agents on normal cells. Furthermore, silymarin and its main bioactive compounds inhibit organic anion transporters (OAT) and ATP-binding cassettes (ABC) transporters, thus contributing to counteracting potential chemo resistance. Silymarin and its derivatives play a double role, namely, limiting the progression of cancer cells through different phases of the cycle—thus forcing them to evolve towards a process of cell death—and accumulating cancer cells in a phase of the cell cycle—thus making it possible to target a greater number of tumor cells with aspecific anticancer agent.Silymarin exerts a chemo preventive effect by inducing intrinsic and extrinsic pathways and reactivating cell death pathways by modulation of the ratio of proapoptotic /antiapoptotic proteins and synergizing with agonists of death domains receptors. In summary, we highlight how silymarin may act as a chemo preventive agent and a chemo sensitizer through multiple pathways.

Angelico R et al., (2019) reviewed the different nano structured systems available in literature as delivery strategies to improve the absorption and bioavailability of silymarin.Silymarin,a mixture of flavonolignan and flavonoid polyphenol compounds extractable from milk thistle (*Silybum marianum*) seeds, has anti-oxidant, anti-inflammatory, anti-cancer and anti-viral activities potentially useful in the treatment of several liver disorders, such as chronic liver diseases, cirrhosis and hepato cellular carcinoma. Equally promising are the effect so silymarin in protecting the brain from the inflammatory and oxidative stress effects by which metabolic syndrome contributes to neurodegenerative diseases. However, although clinical trials have proved that silymarin is safe at high doses (>1500 mg/day) in humans, it suffers limiting factors such as low solubility in water(<50μg/mL), low bioavailability and poor intestinal absorption. To improve its bioavailability and provide a prolonged silymarin release at the site of absorption, the use of nano technological strategies appears to be a promising method to potentiate the therapeutic action and promote sustained release of the active herbal extract.

Literature Review based on Jasmine

Balkrishna A. et al., (2021) reviewed a total of 14 species of Jasminum have been found to be efficient and effective against a wide variety of microbial pathogens. In addition, 14 species were found to be active free radical scavengers. The review is also focused on the disorders related to oxidative stress, and it was concluded that *Jasminum grandiflorum* and *J. sambac* normalized various parameters that were elevated by free radical generation. Alkaloids, flavonoids(rutoside), terpenes, phenols, and iridoid glucosides are among the main phytoconstituents found in various Jasminum species. Furthermore, this review also provides insight into the mechanistic basis of drug resistance, the generation of free radicals, and the role of Jasminum plants in combating resistance and neutralizing free radicals.

DhoteV.etal.,(2021) Explored the cross talk between COX, ROS, and the progression of arthritis.

It was investigated the mechanistic basis of anti-inflammatory activity of the JS concerning RA in CFA induced arthritis model using Lewis rats. A molecular docking study was conducted to correlate the anti-inflammatory activity of JS, where some of the active constituents were docked on the active sites of COX-1 and COX-2 enzyme. These active constituents were identified and selected for COX inhibition based on the available literature. Eight to ten weeks old Lewis rats (n = 40) from the central animal housing facility of the institute were used for the study. In conclusion, JS demonstrated anti-arthritic activity evident from a reduction in paw edema, improvement in ROS scavenging activity, and a decrease in structural damage. Although the vital mechanisms for the observed anti-arthritic activity of JS are COX inhibition and attenuation of oxidative stress, the exploration of the exact role of major signaling pathways is warranted. The completion of the ongoing COX selective in-vitro and in-vivo studies could add more insight into the activity of JS on various chronic inflammatory disorders.

Farouk S. et al., (2021) assessed the bio-acaricidal activity of mustard (*Brassica juncea L.*) fixed oil (MFO), jasmine (*Jasminum grandiflorum L.*) essential oil (JEO), or lavender (*Lavandula angustifolia L.*) essential oil (LEO) and the IR influences on egg-plant growth and productivity. The results demonstrated that JEO represents the most acaricidal properties against TSSM followed by MFO and /or LEO compared to control. Spraying with natural oils significantly improved egg plant growth, i.e., plant height, number of leaves, and branches/plant, in addition to the leaf area and relative leaf dry mass of the 3rd–5th upper leaves. The JEO had the strongest positive effect compared with other oils or control. Additionally, Natural oils application significantly increased photosynthetic pigment, chlorophyll *a:b* ratio, and nitrogen,phosphorus, potassium, ascorbic acid, and phenols. The application of oils increased yield and its quality. In this study, JEO (2.5 mL/l) is shown to be extremely promising for the progress of new eco-friendly acaricides, improving plant growth and increasing egg plant yield.

2.0 Aim &Objectives

Aim

Formulation, evaluation, and characterization of a polyherbal phytosomal gel formulation for Tinea infection

Fungal infections are on the rise, which is concerning. Globally, they cause significant rates of illness and mortality. The prevalence of increasing treatment resistance for fungal infections and the emergence of novel fungus species are on the rise. The current state of antifungal medicines, as well as their side effects, is quite concerning. The reduced fungistatic ability, severe toxicity, and renal failure are all drawbacks of antifungal medications. As a result, it's critical to look for new medicines that might be effective against most fungal infections as alternative treatments. Flavonoids are found in medicinal plants, and they are known to be safe and have a variety of biological activities. Various flavonoids have been isolated and studied in relation to their antifungal properties, and they might be promising, efficient, and cost-effective medicines for preventing fungal infections. By increasing plasma membrane rupture and mitochondrial Mal function, as well as suppressing cell wall construction, cell division, protein synthesis, and the efflux-mediated pumping system, they frequently limit fungal growth. These flavonoids are competent and effective in synergetic combination therapy with conventional medicines, which may be more suited and supportive for the development of new antifungal drug regimens.

Recently, the phospholipid-complex technique has been revealed for addressing these stumbling blocks, namely phytoconstituents, by either increasing their solubilizing capacity or potentiating their ability to pass through biological membranes, as well as protecting active herbal components from degradation. As a result, researchers will be able to transport phytoconstituents into systemic circulation with ease using this phospholipid-complex method. As a result, the goal of this study is to develop a poly-herbal formulation that will more effectively transport active ingredients to treat tinea infections. The produced formulation would allow for regulated medication administration into the deep layers of the skin, improving drug bioavailability and stability while also improving patient compliance.

3.0 Research objectives

The objectives of the study are:

1. To develop herbal formulations with good antifungal activity for various fungal infections.
2. To improve the stability of herbal formulations.
3. To standardize, evaluate the poly-herbal phytosomal gel formulation.
4. To investigate the *in vivo* antifungal properties of prepared phytosomal gel in rabbits.

4.0 Methodology

According to the adopted methodology, the investigation would be divided into four main parts.Pharmacognostic studies, phytochemical studies, pharmaceutical studies, pharmacological studies.

4.1 Pharmacognostical Studies (Standardization)

Organoleptic or macroscopic evaluation:

Organic evaluation of drugs by means of organs of sense (skin, eye, tongue, nose, and ear) or microscopic evaluation, which includes evaluation of drugs by color, odor, taste, size, shape, and special features like touch, texture, etc. It is a technique of qualitative evaluation based on the study of the morphological and sensory profiles of whole drugs.

Microscopic evaluation:

It involves detailed examination of the drugs and can be used to identify the organized drugs by their known histological characters. It is mostly used for qualitative evaluation of organized crude drugs in their entire and purified forms with the help of microscopic evaluation. Using a microscope to detect various cellular tissues, trichomes, stomata, starch granules, calcium oxalate crystals, and aleuronic grains are some of the important parameters that play an important role in the identification of certain crude drugs.

Chemical evaluation:

Most drugs have definite chemical constituents to which their biological or pharmacological activity is attributed. A qualitative chemical test is used to identify a certain drug or to test for impurities. Isolation, purification, and identification of active constituents are based on chemical methods of evaluation.

- Evaluation test of resins: acid value, sulphated ash.

- Evaluation test of balsams: acid value, saponification value, ester value.
- Evaluation test of volatile oils: acetyl and ester values.
- The qualitative chemical tests are useful in the identification of chemical constituents and the detection of adulteration, etc.

4.2 Phytochemical studies

A- Successive Soxhlet extraction

B. Chemical test

1. Chemical test for detection of organic constituents

    - Test for carbohydrates
    - Test for proteins
    - Test for proteins
    - Test for amino acids
    - Test for amino and phenolic compounds.
    - Test for alkaloids
    - Test for glycosides.
    - Test for flavonoids.
    - Test for steroids
    - Test for fats and oils
    - Test for volatile oils

    - Test for phytosterols

4.3 Pharmaceutical Studies

Formulations and evaluation of poly-herbal formulation

Preparation Methods for Phytosomes:

Phytosomes are novel complexes that will be prepared by reacting from 3-2 moles, but preferably with one mole of a natural or synthetic phospholipid, such as phosphatidyl choline, phosphatidyl ethanolamine, or phosphatidyl serine, with one mole of component, for example, flavonolignan, either alone or in the natural mixture in an aprotic solvent such as dioxane or acetone, from which the complex can be isolated by precipitation with a non-solvent, such as aliphatic hydrocarbons, lyophilization, or by spray drying, or by synthesis. The ratio between the two moieties will be in the range of 0.5–2.0 moles. The most preferable ratio of phospholipids to flavonoids is 1:1.

Preparation of Phytosomal gel:

The gelling ingredient for the phytosomal gel would be carbopol 940, which would be distributed in a tiny amount of distilled water and then kept overnight to guarantee full hydration. Then, with constant stirring, preservatives like methyl paraben and propyl paraben will be gently introduced. The produced phytosomes will next be mixed into the gel, resulting in the phytosomal gel. This phytosomal gel would allow for greater herbal extract release and skin penetration.

Evaluation of phytosomes and phytosomal gel:

Evaluation of Phytosomes:

- Characterization technique: visualization, vesicle size and zeta potential, entrapment efficiency, transition temperature, surface tension activity measurement, vesicle stability, and drug content.
- *In vitro* and *in vivo* evaluations
- Stability study

Physical Evaluation of Phytosomal Gel

pH, Viscosity, Homogeneity, Spreadability, Extrudability, Rheology, DSC, FTIR, etc.

4.4 Pharmacological studies

***In vitro* study of polyherbal phytosomal gel**

In vitro release testing (IVRT) is used to monitor the release and diffusion of drug products from semisolid dosage forms and has long been considered a valuable tool in formulation development. IVRT has also been used to screen formulations to select promising candidates, and, importantly, has been accepted for use to obtain a waiver of bioequivalence studies following post approval changes to a product.

Flow-Through Cell Apparatus

In the flow-through method, the test sample is in a small volume cell through which media is pumped at a constant temperature. Upon leaving the cell, the eluate is filtered and can then be analyzed directly or collected in fractions to calculate the percent drug release.

Diffusion cells-

Diffusion cells can be classified as horizontal, vertical, or flow-through based on their physical design. These cells can also be used along with numerous modifications to the basic design. The VDC, recommended by the USP, is one of the more widely accepted apparatuses for in vitro diffusion studies and by far the most commonly used in vitro model for the study of drug release from topical dosage forms.

Immersion cells-

The immersion cell method is similar to the USP paddle-over-disk method, but in this instance, a membrane is used in the immersion cell, which is placed into a USP dissolution vessel.

***In vivo* study of polyherbal phytosomal gel**

Thirty healthy Albino New Zealand rabbits (weight: 1500–500 g each) will be individually housed in suspended cages for 1 week before the experiment. The ethics committee, before the experiment, will approve the experimental protocol. They will be kept in the same environmental and nutritional conditions (temperature of 25 - 2°C, relative humidity of 40%–60%, and 12-hour hours in light and 12 hours in darkness cycles) in the animal house. At the beginning of the

study, animals will be randomly divided into 5 equal groups (n = 6); group [A] will not receive any treatment, [B] will receive a placebo; group [C] will be treated with standard formulation (0.1 mg/ml.kg-1) cream; and group [D] will be treated with standard formulation (0.2 mg/ml.kg-1).[E]Will Inoculated with dermatophyte. 3 cm2 of the albino rabbits' backs will be shaved. Then, after 48 hours, the tested drugs would be applied topically by cotton pad stick on the shaved area of all groups daily, 30 minutes before each UV light exposure. The rabbits would be exposed to UV sunlight (11+ extreme) for 3 hours during each day (temperature: 43± 2°C) for 30 days. All animals will be painlessly killed by chloroform, and samples will be taken from the shaved area for tissue pathology study.

Histopathological Examination

After the *Dermatophyte* challenge on skin, pathogens on the skin will be isolated from the rabbits in the fungal infection (FI) groups 20 days.

1. Fungal observation under microscope would be carried out.
2. Identification of strains would be achieved by polymerase chain reaction (PCR) using the CDR1 gene.
3. The collected anticoagulant blood samples would be analyzed for various blood cell parameters.
4. The levels of antibodies, including IgM and IgA, cytokines, including IL-2, IL-6, and macrophage colony-stimulating factor (M-CSF), and soluble CD4 and CD8 in the serum of the FI group vs. the control group would be determined independently.

RNA isolation from blood samples and fluorescence-based quantitative PCR would be carried out for the mRNA level of *M-csf* 20 days after fungal challenge.

GANTT Chart

S.No.	Details of work	2025									2026												2027					
		4	5	6	7	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12	1	2	3	4	5	6
1	Literature Review																											
2	Authentication of Selected Drugs.																											
3	Pharmacognostical studies.																											
4	Phytochemical studies.																											
5	Pharmaceutical Studies- Formulations and Evaluation of polyherbal formulation.																											
6	Pharmacological Studies- In-vitro study of Poly-herbal Phytosomal gel.																											
8	In-vivo study of Poly-herbal Phytosomal gel.																											
7	Histopathological Examination.																											
8	Dissertation writing & submission.																											

References

[1] Ely JW, Rosenfeld S, Stone MS. Diagnosis and Management of Tinea Infections. Am Fam Physician 2014; 90: 702–710. Im Internet: www.aafp.org/afp.; Stand: 07.07.2021

[2] D H Stein. Tineas-superficial dermatophyte infections - PubMed. . ImInternet https://pubmed.ncbi.nlm.nih.gov/9805462/; Stand: 08.07.2021

[3] Sahoo, Mahajan R. Management of tinea corporis, tinea cruris, and tinea pedis: A comprehensive review. Indian Dermatol Online J 2016; 7: 77. doi:10.4103/2229-5178.178099

[4] Leung AKC, Lam JM, Leong KF, et al. Tinea corporis: An updated review. Drugs Context 2020; 9: 1–12. doi:10.7573/dic.2020-5-6

[5] I W, RC S. The dermatophytes. ClinMicrobiol Rev 1995; 8: 240–259. doi:10.1128/CMR.8.2.240

[6] Agarwal M, Gupta C, Gujral GS, et al. Tineacorporis infection manifestating as retinochoroiditis—an unusual presentation. J Ophthalmic Inflamm Infect 2019; 9. doi:10.1186/s12348-019-0173-z

[7] BP K. Superficial fungal infections. Pediatr Rev 2012; 33. doi:10.1542/PIR.33-4-E22

[8] O D, MD D, KB R, et al. Incidence of cutaneous lupus erythematosus, 1965-2005: a population-based study. Arch Dermatol 2009; 145: 249–253. doi:10.1001/ARCHDERMATOL.2009.21

[9]. Rahman HS, Othman HH, Hammadi NI, et al. Novel Drug Delivery Systems for Loading of Natural Plant Extracts and Their Biomedical Applications. 2020. doi:10.2147/IJN.S227805

[10].Soib HH, Fahmi Ismail H, Husin F, et al. molecules Bioassay-Guided Different Extraction Techniques of Carica papaya (Linn.) Leaves on In Vitro Wound-Healing Activities.Molecules 2020; 25: 517. doi:10.3390/molecules25030517

[11] D D, T E-M, K C, et al. Melissa officinalis ssp. altissima extracts: A therapeutic approach targeting psoriasis in mice. J Ethnopharmacol 2020; 246. doi:10.1016/J.JEP.2019.112208

[12] Huang T-H, Lin C-F, Alalaiwe A, et al. Molecular Sciences Apoptotic or Antiproliferative Activity of Natural Products against Keratinocytes for the Treatment of Psoriasis. Int J Mol Sci 2019; 20: 2558. doi:10.3390/ijms20102558

[13] M D, M A, R Z, et al. Progress and prospects in the management of psoriasis and Developments in phyto-therapeutic modalities. DermatolTher 2019; 32. doi:10.1111/DTH.12866

[14]Molaveisi M, ShahidiNoghabi M, Parastouei K, et al. Fate of nano-phytosomes containing bioactive compounds of Echinacea extract in an acidic food beverage. Food Struct 2021; 27: 100177. doi:10.1016/J.FOOSTR.2021.100177

[15] Ebada HMK, Nasra MMA, Elnaggar YSR, et al. Novel rhein integrate transphytosomes as non-invasive local therapy for osteoarthritis to ameliorate cartilage deterioration in MIA-arthritic rats. Colloids Surfaces B Biointerfaces 2021; 202: 11171doi:10.1016/J.COLSURFB.2021.111713

[16] Zhu S, Luo C, Feng W, et al. Selenium-deposited tripterinephytosomes ameliorate the antiarthritic efficacy of the phytomedicine via a synergistic sensitization. Int J Pharm 2020; 578: 119104. doi:10.1016/J.IJPHARM.2020.119104

[17]Delmas D, Xiao J, Vejux A, et al. molecules Silymarin and Cancer: A Dual Strategy in Both in Chemoprevention and Chemosensitivity. . doi:10.3390/molecules25092009

[18] Di Costanzo A, Angelico R. Formulation strategies for enhancing the bioavailability of silymarin: The state of the art. Molecules 2019; 24: 1–29. doi:10.3390/molecules24112155

[19] Balkrishna A, Rohela A, Kumar A, et al. plants Mechanistic Insight into Antimicrobial and Antioxidant Potential of Jasminum Species: A Herbal Approach for Disease Management. 2021. doi:10.3390/plants

[20] Dhote V, Dangi U, Mandloi AS, et al. Preferential cyclooxygenase inhibition by Jasminumsambac: A possible relationship with potent anti-arthritic activity. J Tradit Complement Med 2021; 11: 217. doi:10.1016/J.JTCME.2020.04.002

[21] Farouk S, Almutairi AB, Alharbi YO, et al. Acaricidal Efficacy of Jasmine and Lavender Essential Oil or Mustard Fixed Oil against Two-Spotted Spider Mite and Their Impact on Growth and Yield of Eggplants. 2021. doi:10.3390/biology10050410

[22] Arvind SB, Manoj GS, Snehal PR, et al. Standardization of herbal drugs: An overview. PharmaInnov J 2015; 100: 100–104. Im Internet: www.thepharmajournal.com; Stand: 28.07.2021

[23] Harborne JB (Jeffrey B. Phytochemical methods: a guide to modern techniques of plant analysis. 1998: 302

[24] Pharmacological methods in phytotherapy research: volume 1: Selection, preparation and pharmacological evaluation of plant material. . Im Internet: https://agris.fao.org/agris-search/search.do?recordID=GB9719304; Stand: 28.07.2021

[25] Li N, Lin G, Kwan YW, et al. Simultaneous quantification of five major biologically active ingredients of saffron by high-performance liquid chromatography. J Chromatogr A 1999; 849: 349–355. doi:10.1016/S0021-9673(99)00600-7

[26] (14) (PDF) Standardization and quality evaluation of herbal drugs. . Im Internet: https://www.researchgate.net/publication/308376096_Standardization_and_quality_evaluation_of_herbal_drugs; Stand: 28.07.2021

[27]Djekic L, Krajišnik D, Mićic Z, et al. Formulation and physicochemical characterization of hydrogels with 18β-glycyrrhetinic acid/phospholipid complex phytosomes. J Drug Deliv Sci Technol 2016; 35: 81–90. doi:10.1016/J.JDDST.2016.06.008

[28]M. Sravanthi* and J. Shiva Krishna. PHYTOSOMES: A NOVEL DRUG DELIVERY FOR HERBAL EXTRACTS | INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH. 2013. Im Internet: https://ijpsr.com/bft- article/phytosomes-a-novel-drug-delivery-for-herbal-extracts/; Stand: 21.07.2021

[30] Joshua JM, Anilkumar A, Verjina CU, et al. Formulation and evaluation of antiagingphytosomal gel. Asian J Pharm Clin Res 2018; 11: 409–422. doi:10.22159/AJPCR.2018.V11I3.24257

[31]Altaei T. The treatment of melasma by silymarin cream. 2012. doi:10.1186/1471-5945