Review Article

A Novel Approach of Natural Nanoparticulate System for Psoriatic Skin Care

Syed Gouse Firoz[1], A. Arun Kumar [2], N. Adilakshmi[3], K. Sudha Rani[4], A. Venkata Padma[5], S. Jagan Mohan[6], M. Ramya Brahmini[7]
[1] Department of pharmaceutics, AM Reddy Memorial college of pharmacy, Petlurivaripalem, Narasaraopet, Palnadu-522601 Andra Pradesh, India.
[2,3,4,5,6,7] B. Pharm Students AM Reddy memorial college of pharmacy, Petlurivaripalem, Narasaraopet, Palnadu-522601 Andra Pradesh, India.
***Corresponding author's E-mail:** arunkumar.abbireddy1@gmail.com

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ABSTRACT

Psoriasis is a chronic autoimmune skin disorder characterized by red scaly plaques that can cause significant discomfort and impact the quality of life. Traditional topical treatments often fall short in terms of efficacy and patient compliance due to limited drug penetration and potential skin irritation. This study explores a novel approach using natural nanoparticulate systems to enhance the delivery and efficacy of herbal extracts for psoriatic skin care. The research focuses on the formulation of lipid-based nanoparticles (SLNs and NLCs), polymeric nanoparticles and nano-emulsions incorporating bioactive compounds from Annona squamosa (custard apple). These natural nanoparticles are designed to improve drug stability, penetration and controlled release targeting the affected skin areas more effectively. *In vitro* release and stability testing cytotoxicity and skin irritation studies are conducted to evaluate the safety and efficacy of these formulations. The results demonstrate that natural nanoparticulate systems can significantly enhance the therapeutic potential of Annona squamosa extracts offering a promising alternative for psoriatic skin care.

Keywords: Nanoparticles, Herbal extracts, Annona squamosa extracts, controlled release system.

INTRODUCTION

Nanoparticles (10–1000 nm) are tiny drug carriers that can be solid or dispersed, with drugs incorporated in various ways. They exist as nanoparticles, nanospheres, or nano capsules. [1]

Nano capsules are like tiny drug-filled bubbles, where the medication is confined within a cavity surrounded by a unique polymer membrane. On the other hand, nanospheres have the drug physically and uniformly dispersed throughout the matrix. [1]

Biodegradable polymeric nanoparticles, especially those coated with hydrophilic polymers like polyethylene glycol (PEG), have indeed gained significant attention in recent years for their potential in drug delivery systems. [17]

These are known as long-circulating particles because they can stay in the bloodstream for extended periods, target specific organs, and deliver DNA in gene therapy. They are also effective in delivering proteins, peptides, and genes, making them a versatile tool in modern medicine. [1]

PSORIASIS:

Psoriasis is a chronic autoimmune condition that causes inflammation and rapid skin cell turnover, leading to the formation of thick, scaly patches on the skin. [18] It's not just about dealing with skin issues people with psoriasis often face other serious health problems, including joint pain (psoriatic arthropathy) psychological challenges and heart and liver conditions. [2] Psoriasis is like that It's a chronic skin disease that can show up at any age and affects people worldwide. It causes red, itchy patches covered with silvery scales, often appearing on the elbows, knees, scalp, and lower back. [3]

PSORIASIS OVERVIEW:

Psoriasis doesn't discriminate, it affects both men and women. Interestingly, women and those with a family history of the condition tend to experience it earlier. For men, the age of onset often peaks between 30-39 years and 60-69 years, whereas for women, it tends to occur about ten years earlier. [2]

Globally, around 60 million people live with psoriasis. The prevalence of psoriasis varies significantly from country to country, with as few as 0.05% of the population affected in Taiwan to as many as 1.88% in Australia.[19]It tends to be more common in high-income regions and among older populations. In the UK, about 1.52% of the general population deals with this condition. [3]

TYPES OF PSORIASIS:

1. **Guttate Psoriasis:**

It is a form of psoriasis that tends to affect children and young adults. It is characterized by small, drop-shaped lesions that appear on the skin. This type of psoriasis often occurs suddenly and can be triggered by infections such as strep throat. [4]These lesions can also manifest as scaly psoriatic papules, usually following a streptococcal infection (like strep throat). This form of psoriasis is commonly linked to the HLA-Cw6 gene, and often, ant streptolysin titters are elevated in these cases.

Interestingly, as the infection subsides, the lesions usually disappear on their own. You'll typically find these lesions on the trunk, upper arms, face, and scalp. The good news is, they generally fade away within 3-4 months. However, sometimes these lesions can grow and take the shape of psoriatic plaques. [5]

Figure 1: Psoriasis affecting the skin on both forearms, characterized by red, scaly patches.

Figure 2: Different manifestations of psoriasis on various body parts, including the scalp, back, nails, hands, knees, and face.

Flexural or Inverse Psoriasis:

Flexural or inverse psoriasis refers to a type of psoriasis that affects the skinfolds, such as under the breasts, in the armpits, around the groin, and other areas where skin touches skin. [19]Instead, the lesions appear as bright red, symmetric, and infiltrative plaques with distinct, sharp contours. These plaques can be fissured, making this form of psoriasis quite diagnostic. [5]

This type of psoriasis is more commonly seen in obese individuals and tends to be associated with seborrheic lesions. [5]

2. **Erythrodermic Psoriasis**: -

It is a severe form of psoriasis that can affect up to 80% of the body's surface area. Instead of the typical papules and plaques, you'll see predominantly red (erythematous) lesions that lose their characteristic features. The skin peeling (desquamation) isn't as noticeable in this form. [5]

3. **Guttate Psoriasis:**

Guttate psoriasis is characterized by the sudden onset of numerous small (1–10 mm) red papules, often covered with fine scales. It is more commonly found in children and young adults and accounts for less than 2% of all psoriasis cases.

4. **Pustular Psoriasis:**

Characterized by white pustules (blisters of non-infectious pus) surrounded by red skin. [5]

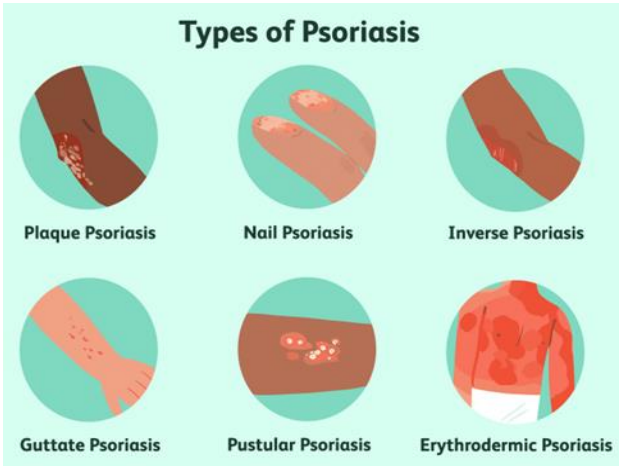

Figure 3: Different types of Psoriasis

SYMPTOMS: -

- ✓ Red, inflamed skin
- ✓ Thick, silvery scales
- ✓ Itching, burning, or soreness
- ✓ Dry, cracked skin that may bleed
- ✓ Nail changes (pitting, discoloration, or separation from the nail bed)
- ✓ Joint pain (psoriatic arthritis, which affects some individuals with psoriasis)

CAUSES AND RISK FACTORS:

Psoriasis is an autoimmune condition that affects how the immune system works. Normally, the immune system produces T cells to protect the body from infections. In someone with psoriasis, certain triggers can cause the immune system to mistakenly attack healthy skin cells. It's as if the T cells think they are fighting an infection or healing a wound, and they start producing chemicals that cause inflammation. [6]

This autoimmune activity leads to the rapid growth of skin cells, which then build up and form those characteristic plaques seen in psoriasis. [6]

- ➢ Infections (e.g., strep throat or skin infections)
- ➢ Stress
- ➢ Skin injuries (e.g., cuts, bug bites, or sunburns)
- ➢ Certain medications
- ➢ Weather (extreme cold or dry conditions)
- ➢ Smoking and alcohol consumption

DIAGNOSIS AND TREATMENT:

The diagnosis of psoriasis is primarily based on clinical evaluation. Chronic plaque psoriasis is the most common type, affecting 80% to 90% of psoriasis patients. It is characterized by well-demarcated, symmetric, erythematous plaques with overlying silvery scales, typically found on the scalp, trunk, buttocks, and extremities. Nail involvement can occur, even without concomitant plaques. Active lesions may be itchy or painful. Psoriasis can also present as an isomorphic response, where new lesions develop on previously normal skin after trauma or injury. [7]

- **Topical treatments:** Steroid creams, vitamin D analogise, and moisturizers.
- **Phototherapy:** Exposure to ultraviolet light under medical supervision.
- **Systemic treatments:** Oral or injectable medications, such as biologics and immunosuppressants, for moderate to severe cases.
- **Lifestyle modifications:** Managing triggers, stress reduction, and adopting a skin-care routine to prevent flare-ups. [7]

MEDICATIONS USED IN PSORIAIS TREATMENT: -

1. **Topical Corticosteroids:** Hydrocortisone, betamethasone, and clobetasol propionate.
2. **Vitamin D Analogues:** Calcipotriene and calcitriol.
3. **Topical Retinoids**: Tazarotene and adapalene.
4. **Coal Tar:** Used to reduce inflammation and slow down skin cell growth. [8]
5. **Methotrexate:** Oral medication used to slow down skin cell growth and reduce inflammation.
6. **Cyclosporine:** Oral medication used to suppress the immune system and reduce inflammation.
7. **Biologics:** Adalimumab, etanercept. [9]

HERBAL NANO PARTICULATE DRUG DELIVERY SYSTEM: -
Nanoparticles are increasingly used in herbal drug delivery to improve bioavailability, stability, and targeted delivery. Here are the key types:

1. Lipid-Based Nanoparticles:

- **Solid Lipid Nanoparticles (SLNs):**

Composed of solid lipids stabilized by surfactants, they provide controlled drug release and improved drug stability. Due to their small size (50-1000 nm) and biocompatibility, SLNs have diverse applications in pharmaceuticals, suitable for various administration routes such as parenteral, oral, and percutaneous. The process involves melting the solid lipid and incorporating the drug into it, followed by stabilization with surfactants. [10]

- **Nanostructured Lipid Carriers (NLCs):**

Modified SLNs containing liquid and solid lipids, enhancing drug loading and minimizing leakage. [10]

2.Polymeric Nanoparticles:

These can be made from natural polymers extracted from the plant, such as cellulose or chitosan, to encapsulate bioactive compounds from Annona squamosa. [11]

3.Nanoemulsions:

These are emulsions with droplet sizes in the nanometre range, which can be prepared using the oil extracted from Annona squamosa fruit pulp. [11]

4.Micelles:

These can be formed using amphiphilic molecules derived from the plant, which can encapsulate hydrophobic compounds from Annona squamosa. [11]

5.Nanocapsules:

These consist of a core-shell structure where the core contains the herbal extract from Annona squamosa, and the shell is made from natural or synthetic polymers. [11]

6.Phytosomes:

These are complexes of standardized plant extracts or water-soluble phytoconstituents with phospholipids, enhancing the solubility and bioavailability of herbal drugs from Annona squamosa. [11]These nanoparticles can be used for various applications, including antimicrobial, antioxidant, and anticancer activities, leveraging the natural bioactive compounds present in Annona squamosa. [12]

CHEMICAL CONSTITUENTS: -

Annona squamosa seed oil (ASO) contains 6.7 ± 0.2% moisture, 26.8 ± 0.4% fat, 17.2± 0.2 % protein,2.2 ± 0.1 % Ash, 16.8 ± 0.2 % Fiber, 30.0 ± 0.3 % CHO, Acetogenin.

Uses: -

- Acetogenin used as anthelmintic agent
- Oil extracted from seeds of Annona squamosa was used to get rid from head lice. Seed extracted oil has been used in agriculture as a pesticidal agent.
- petroleum ether extract of seeds of Annona squamosa as an anti-psoriatic agent

METHODS FOR DEVELOPING USING NANOPARTICLES: -

EXTRACTION OF ANNOVA SQUAMOSA LEAVES: -

The leaves of Annova squamosa were thoroughly cleaned with water to remove dust particles and shade-dried at room temperature and reduced to coarse powder using a mechanical mixer.[13]

To prepare the Annona squamosa leaf extract, the collected leaves were first washed thoroughly 2-3 times with fresh water to ensure cleanliness and eliminate any potential

inconsistencies. Once clean, the leaves were allowed to dry completely before being ground into a fine powder.[14]

Weighing out 5 grams of this powdered leaf material, we mixed it with 100 millilitres of deionized water in a beaker. The mixture was then placed on a hot plate and brought to a boil. For the next 25-30 minutes, the solution was continually stirred while maintaining the boiling temperature.[14]

After the boiling process, the mixture was filtered using Whatman filter paper to remove any solid particles, resulting in a clear leaf extract.[14]

Figure- 4: Leaves of a plant species, showcasing their elongated shape and prominent veins.

EXTRACTION BY USING SEEDS: -The fruit pulp and seeds were manually separated, washed with water and air dried. For preparation of extracts, dried seeds of Annona squamosa were grounded to powder using an electrical mixer blender. 100 ml Petroleum ether was added into 50 g of the powdered seeds and extraction was carried out at room temperature (RT) for 24 h. The extract was filtered with Whatman filter paper and the residue was further kept in fume cupboard for 72 h for complete removal of petroleum ether. The resultant Annona squamosa seed oil (ASO) was stored at RT for subsequent analysis.

Figure 5: Leaves of the plant

1.**Nanoparticle Synthesis:**

- **Nanoprecipitation**: The leaf extract was dissolved in a solvent and then precipitated by adding a non-solvent, forming nanoparticles with a narrow size distribution. [11]
- **Solvent Evaporation**: The extract was dissolved in a volatile organic solvent, which was evaporated to leave behind nanoparticles, suitable for encapsulating both lipophilic and hydrophilic compounds.
- **High-Pressure Homogenization:** High shear forces were applied to break down the extract into nanoparticles, producing stable and uniform particles.[11]

Figure 6: Custard apple (Annona squamosa) with a cross-section showing its creamy white flesh and black seeds.

2. Formulation of Herbal Nanoparticles:

- **Lipid-Based Nanoparticles**: Solid Lipid Nanoparticles (SLNs) and Nanostructured Lipid Carriers (NLCs) were formulated using lipids extracted from the fruit pulp of *Annona squamosa*.
- **Polymeric Nanoparticles**: These were made from natural or synthetic polymers, providing controlled release of the herbal extract.
- **Nano emulsions**: Emulsions with droplet sizes in the nanometre range were prepared using the oil extracted from the fruit pulp.
- **Micelles**: Formed by self-assembly of amphiphilic molecules derived from the plant, encapsulating hydrophobic compounds.
- **Nano capsules**: These had a core-shell structure with the herbal extract in the core and a polymer or lipid shell.
- **Phytosomes**: Complexes of standardized plant extracts or water-soluble phytoconstituents with phospholipids, enhancing solubility and bioavailability.

3. Surface Modification and Functionalization:

- **PEGylation and Surface Coating**: Polyethylene glycol (PEG) and other coatings were applied to enhance stability and reduce immunogenicity.
- **Targeted Delivery via Ligand Conjugation**: Ligands were attached to the nanoparticle surface to target specific skin cells, improving treatment efficacy.[11]

4. Skin Penetration Enhancement:

- **Use of Penetration Enhancers**: Compounds such as surfactants and fatty acids were used to enhance nanoparticle penetration through the skin.
- **Microneedle or Electroporation Techniques**: These techniques created microchannels in the skin, facilitating nanoparticle entry.

5. Characterization and Evaluation:

- **Particle Size and Morphology Analysis**: Techniques such as Dynamic Light Scattering (DLS) and Scanning Electron Microscopy (SEM) characterized the size and shape of the nanoparticles.
- **In Vitro Release and Stability Testing**: The release profile and stability of the nanoparticles were evaluated using in vitro techniques.
- **Cytotoxicity and Skin Irritation Studies**: These studies ensured the safety of the nanoparticles for topical application. [11]

EVALUATION OF NANOPARTICLES IN ANNOVA SQUMASA:

Evaluation Methods for Herbal Nanoparticles Using *Annona squamosa*

1. Particle Size and Morphology Analysis:

- **Dynamic Light Scattering (DLS)**: Measures the size distribution of nanoparticles in a solution.
- **Scanning Electron Microscopy (SEM)**: Provides detailed images of the nanoparticle surface and morphology. [11]
- **Transmission Electron Microscopy (TEM)**: Offers high-resolution images to observe the internal structure of nanoparticles. [11]

2. Zeta Potential Measurement:

- Determines the surface charge of nanoparticles, which affects their stability in suspension. [11]

3. Fourier Transform Infrared Spectroscopy (FTIR):

- Identifies the functional groups present on the nanoparticle surface, confirming the successful incorporation of herbal extracts. [11]

4. X-ray Diffraction (XRD):

- Analyses the crystalline structure of nanoparticles, providing information on their composition and phase. [11]

5. In Vitro Release Studies:

- Assesses the release profile of the active compounds from the nanoparticles over time using simulated body fluids. [11]

6. Stability Studies:

- Evaluates the physical and chemical stability of nanoparticles under different storage conditions (temperature, humidity, light exposure). [11]

7. Cytotoxicity and Skin Irritation Studies:

- Conducted to ensure the safety of nanoparticles for topical application, using cell culture assays and skin models. [11]

8. Antimicrobial Activity Testing:

- Assesses the effectiveness of nanoparticles against various microbial strains using methods like disc diffusion and broth dilution. [11]

9. Antioxidant Activity Assay:

- Measures the antioxidant capacity of nanoparticles using assays such as DPPH radical scavenging and ABTS assays. [11]

10. Targeted Delivery Efficiency:

- Evaluates the ability of nanoparticles to target specific cells or tissues, often using fluorescent labeling and imaging techniques. [11]

Uses: -

1) Antioxidant Properties
2) Anticancer Activity
3) Antidiabetic Effect
4) Antimicrobial Activity
5) Hepatoprotective Effects
6) In traditional medicine, the leaves are used to treat various ailments such as diabetes, inflammation, and digestive issues.

CONCLUSION

In conclusion, the natural nanoparticulate systems formulated with Annona squamosa extracts offer a promising alternative for the treatment of psoriasis. These innovative formulations enhance drug stability, penetration, and controlled release, thereby improving therapeutic efficacy and patient compliance. The use of natural compounds combined with advanced nanotechnology provides a safer and more effective approach for psoriatic skin care. Further research and clinical trials are warranted to fully realize the potential of these novel treatments in managing psoriasis.

FUTHER AND CURRENT DIRECTIONS

Current Research on *Annona squamosa* Nanoparticles: -

Recent studies have focused on the green synthesis of nanoparticles using *Annona squamosa* leaf extract due to its natural phytochemicals. These nanoparticles have shown promising antibacterial and antioxidant properties. For instance, research has demonstrated the effectiveness of silver nanoparticles synthesized using *Annona squamosa* extract against various bacterial strains.[15]

Future Directions in Nanoparticle Research:

1. **Personalized Nanomedicine**: Developing nanoparticles tailored to individual patients' needs, enhancing treatment efficacy.[16]
2. **Smart Nanoparticles**: Creating nanoparticles that respond to environmental stimuli, improving targeted drug delivery.[16]
3. **Theramostic Nanoparticles**: Combining diagnostic and therapeutic functions in a single nanoparticle for more efficient treatment.[16]
4. **Biodegradable Nanoparticles**: Focusing on eco-friendly nanoparticles that minimize environmental impact.[16]
5. **Integration of AI**: Using artificial intelligence to optimize nanoparticle design and improve manufacturing processes.[16]

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