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Review Article

A Complete Assessment on Herbal Antiaging Nanogels Using Different Fruits

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ABSTRACT

Herbal cosmetic nanogels represent a novel and promising formulation strategy that combines the therapeutic benefits of herbal ingredients with the advanced delivery capabilities of nanotechnology. The incorporation of fruit-derived bioactives into nanogel systems has garnered significant attention in recent years due to the rich content of vitamins, antioxidants, enzymes, and natural acids found in fruits, which offer a wide range of skin benefits. Herbal nanogels are an advanced drug delivery system that combines the therapeutic benefits of herbal medicines with the technological advantages of nanotechnology. They represent a promising area of research in pharmaceutical sciences and natural product therapy due to their potential to enhance the bioavailability, stability, and targeted delivery of herbal drugs. Nanogels, being nanoscale hydrogel systems, allow for enhanced skin penetration, controlled release, and improved stability of sensitive fruit actives. Fruits such as papaya (*Carica papaya*), orange (*Citrus sinensis*), pomegranate (*Punica granatum*), strawberry (*Fragaria ananassa*), and grape (*Vitis vinifera*) are commonly used in cosmetic nanogels for their skin-brightening, anti-aging, exfoliating, and antioxidant properties. These nanogels are typically prepared using natural or synthetic polymers like Carbopol or chitosan, with the fruit extract incorporated via nanoemulsion or ionic gelation techniques. The resulting nanogel formulations are non-greasy, easy to apply, and cosmetically elegant, making them highly suitable for facial care, anti-acne, anti-aging, and skin-rejuvenating products. Preliminary evaluations indicate high consumer acceptability, improved bioactivity of fruit components, and minimal skin irritation. Thus, herbal cosmetic nanogels containing fruit extracts offer a natural, effective, and safe alternative to synthetic cosmetic products, aligning with the rising demand for green and sustainable skin care solutions.

INTRODUCTION

Nanogels are nanoscale, three-dimensional, hydrophilic polymer networks capable of holding

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large amounts of water or biological fluids. They are typically in the size range of 20–200 nm and are composed of natural or synthetic polymers.

Herbal nanogels are nanogel formulations that incorporate herbal extracts or phytoconstituents (active plant compounds) for therapeutic applications. By combining herbal bioactive with nanotechnology, the formulation improves the solubility, absorption, and efficacy of herbal drugs, which are often limited by poor water solubility and low bioavailability.

Advantages of Herbal Nanogels

- **Improved Bioavailability:** Nanogels enhance the solubility and permeability of herbal compounds.
- **Controlled and Targeted Delivery:** They provide sustained release and can be engineered for site-specific delivery.
- **Reduced Side Effects:** Targeted delivery minimizes the exposure of non-target tissues.
- **Stability of Herbal Extracts:** Nanogels protect sensitive herbal components from degradation.
- **Non-Invasive Application:** Often used topically, offering patient-friendly delivery methods.

Applications of Herbal Nanogels

- **Dermatology:** Treatment of acne, eczema, psoriasis, and skin infections
- **Anti-inflammatory:** Delivery of herbal anti-inflammatory agents
- **Antimicrobial:** Enhanced antimicrobial activity due to nano-size and herbal synergy

- **Cancer therapy:** Potential use in delivering herbal anticancer agents
- **Herbal cosmetic nanogels** are nano-sized hydrogel formulations that incorporate plant-based active ingredients intended for cosmetic or dermatological purposes. These nanogels are non-greasy, highly spreadable, and capable of delivering herbal compounds deeper into the skin layers, resulting in improved cosmetic benefits¹.

Nanogels improve the delivery, efficacy, and aesthetic appeal of herbal cosmetics due to:

- Enhanced skin absorption
- Controlled and sustained release of actives
- Non-comedogenic (doesn't clog pores)
- Transparent or translucent appearance (good for cosmetic appeal)
- Cooling, soothing texture ideal for skin application

Use of Fruits in Nanogels:

Fruits are rich in:

- **Antioxidants** (Vitamin C, E, polyphenols)
- **Natural AHA/BHAs** (exfoliants)
- **Flavonoids & Enzymes** (brightening, anti-inflammatory)
- **Vitamins & Minerals** (nourishment)
- They provide:
 - **Anti-aging** properties
 - **Skin brightening**



- **Moisturizing effects**

Examples of Fruits for Nanogel Formulation

- **Anti-acne or soothing action².**

Fruit	Active Compounds	Benefits	Use in Nanogels
Papaya	Papain enzyme, Vit A & C	Exfoliating, brightening	Anti-acne, glow gel
Pomegranate	Punicalagin, antioxidants	Anti-aging, collagen booster	Anti-wrinkle gel
Strawberry	Alpha-hydroxy acids, Vit C	Skin renewal, lightening	Peel-off or night gel
Banana	Potassium, Vit B6, antioxidants	Moisturizing, softening	Hydrating day gel
Lemon	Citric acid, Vit C	Lightening, antibacterial	Spot-correction gel
Aloe Vera (herbal)	Polysaccharides, enzymes	Soothing, healing	Base + synergy with fruits
Cucumber	Flavonoids, water content	Cooling, anti-puffiness	Eye gel or face gel

Mechanism Of Drug Release from Nanogels

- pH stimulus
- Degradation of nanogel
- Ionic exchange with environment
- Simple diffusion
- From external energy sources

The release by stimulation of pH from the gel is the result of side group ionization. Nanogel polymers are composed of anionic or cationic side groups. In an aqueous environment, these groups will ionize at the appropriate pH and ionic strength. This creates a fixed charge on the polymer, causing electrostatic repulsion, which enlarges the pores of the gel. As a result, the flow of water into the gel increases, leading to swelling of the nanogel and drug release. The degradable nature of the nanogel ensures low toxicity and prevents unnecessary accumulation after repeated administration. Easily cleavable bonds can be introduced into the polymer backbone. Degradation is for specific reducing compounds,

pH or even enzymatic activity. The lowest critical solution temperature (LCST) of the thermosensitive nanogel poly(N-isopropylacrylamide) in an aqueous medium is 32°C. At a temperature lower than the LCST, the amide group of the polymer interacts with the hydrogen of water, so the polymer is hydrated. When the temperature increases, the hydrophobic interaction of the polymer becomes obvious. The hydrogen bond with water is broken, the water phase separates and nanogel aggregation occurs; thereby releasing the captured drug into the environment. The diffusion release of the drug from the gel is the result of the difference in environmental concentration. The drug moves from the higher concentration area (inside the gel) to the lower concentration area (around). Another method is displacement by ions which is present in environment. A lot of research work is developing nanogels that can release biological agents in response to environmental cues at specific sites of action. When a cationic nanogel containing a negatively charged drug interacts with negatively charged particles in the environment/cell surface, the drug will be exchanged for negatively charged particles³.



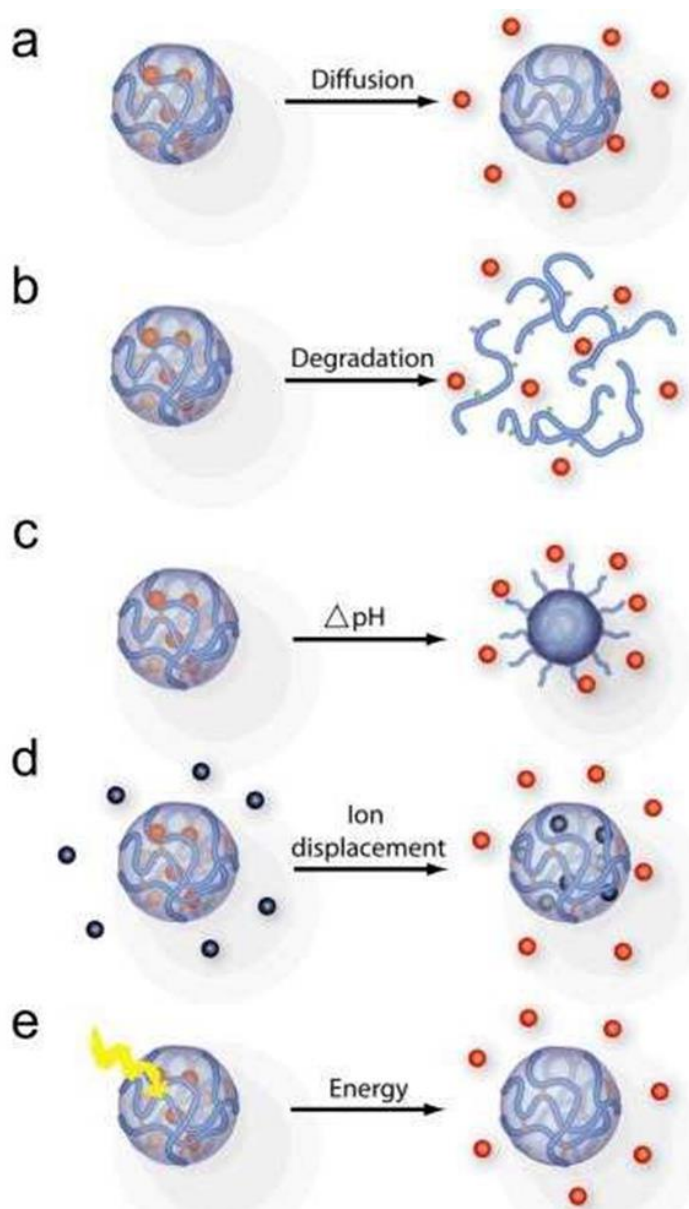


Image 1: Mechanism of drug release from Nanogels

MATERIALS AND METHODS

Preparation Methods of Herbal Cosmetic Nanogels

- Emulsion-solvent evaporation
- Ionic gelation
- Nanoprecipitation
- Reverse micelle technique

- High-energy methods (ultrasonication, high-pressure homogenization)

Preparation of Herbal Cosmetic Nanogels

The preparation of herbal cosmetic nanogels involves two major steps:

- Formulation of herbal nanoparticles or nanoemulsions (containing herbal extracts)

- Incorporation into a gel base to form a nanogel suitable for topical application.

The methods and steps involved in preparing herbal cosmetic nanogels.

Selection of Materials

a. Herbal Extract / Phytoconstituent

- Plant-based actives (e.g., aloe vera, neem, turmeric, green tea)
- Can be aqueous, alcoholic, or hydroalcoholic extracts

b. Polymers / Gelling Agents

- Natural: Chitosan, xanthan gum, guar gum
- Synthetic: Carbopol 934, Hydroxypropyl methylcellulose (HPMC)

c. Solvents

- Distilled water, ethanol, or hydroalcoholic mixtures

d. Surfactants / Stabilizers (for nanoemulsions)

- Tween 80, Span 60, lecithin (for emulsification and stabilization)⁴

Formulation:

A. Nanoemulsion - Based Nanogels

Formulation of Nanoemulsion:

- Dissolve herbal extract in the oil phase or aqueous phase.
- Add surfactants and co-surfactants.

- Use high-speed homogenization or ultrasonication to reduce particle size (<200 nm).

Incorporation into Gel Base:

- Prepare the gel base using gelling agents like Carbopol in water.
- Neutralize (e.g., with triethanolamine) to form gel.
- Add the nanoemulsion slowly into the gel with continuous stirring.

B. Ionic Gelation Method (for nanoparticle-based nanogels)

Synthesize Nanoparticles:

- Mix herbal extract with a polymer (e.g., chitosan).
- Add a cross-linker (e.g., sodium tripolyphosphate) under stirring.
- Nanoparticles form via ionic interaction.

Disperse Nanoparticles into Gel Base:

- Prepare gel with agents like HPMC or Carbopol.
- Disperse the nanoparticle suspension into the gel base.

C. Sol-Gel Technique (Simple Herbal Nanogel Preparation)

- Dissolve the herbal extract in a suitable solvent.
- Mix with gelling agent (e.g., Carbopol) under gentle stirring.
- Allow to swell and neutralize to form a gel.



- Use ultrasonication to reduce particle size and ensure uniformity^{5,6,7}.

Evaluation Parameters

After formulation, the herbal cosmetic nanogel should be evaluated for:

- pH
- Viscosity
- Spreadability
- Particle size and distribution
- Drug content
- Skin irritation or compatibility
- Stability (over time, temperature, light)⁸

Evaluation Of Nanogel:

a) Appearance: The prepared nanogel were inspected visually for clarity, colour and the presence of any particles.

b) pH: The pH of the all nanogel was determined using digital pH meter. about 1 gm of nanogel was stirred in distilled water till a uniform suspension effected. The volume was made upto 50 ml and pH of the solution was measured.

c) Homogeneity: All developed nanogels were tested for homogeneity by visual inspection after the nanogels have been set in the container. They were tested for their appearance and presence of any aggregates⁹.

d) Rheological properties: Rheological properties (study of deformation and flow of matter) are required in various pharmaceutical areas. some of the reasons for determining these properties are. • It helps in understanding the physicochemical

nature of vehicle and quality control of ingredients, test formulations and final products, together with the manufacturing process such as mixing, pumping and filling. • It reflects the effects such as temperature and storage time on the products. • It helps to access a topical formulation with respect to the patient usage e.g. removal of the preparation from a jar or tube without spillage or spreadability and adherence to skin¹⁰.

• Finally, it helps to monitor the effects of vehicles consistency on the release of drug from the preparation and its subsequent percutaneous absorption¹¹.

e) Spreadability: Spreadability is determined by apparatus suggested by Mutimer. It consists of wooden block, which is provided by a pulley at one end. By this method, spreadability is measured on the basis of “Slip” and “Drag”. A ground glass slide is fixed on this block. A sample of 0.1 g of nanogel under study is placed on this ground slide. The gel is fixed on the beach formula was pressed between two slides and a 1 kg weight is placed on the top of two slides and left for about 5 min to expel air and to provide a uniform film of the nanogel between two slides. Excess of the gel is scrapped from edges. The top plate is then subjected to pull the weight. With help of string attaches to the hook and the time required by top slide to cover the distance is noted. A shorter interval indicates better spreadability¹².

Spreadability was calculated by using the formula,

$$S = M.L/T,$$

Where,

S = Spreadability,

L = Length of glass slide,



M = Weight tied to upper slide,

T = Time taken to separate the slides¹³.

f) Extrudability: It is a usual empirical test to measure the force required to extrude the material from tube. The method applied for determination of applied shear in the region of the rheogram corresponding to a shear rate exceeding the yield value and exhibiting plug flow. The method adopted for evaluating nanogel formulation for extrudability is based upon the quantity in percentage of nanogel and nanogel extruded from lacquered aluminium collapsible tube on application of weight in grams required at least 0.5cm ribbon of nanogel in 10 sec. The measurement of extrudability of each formulation shows the triplicate and averages value is presented.

Extrudability = Applied weight to extrude the nanogel from tube (in gm)/ Area (in cm²)¹⁴.

g) Rheological Studies (viscosity): Brookfield viscometer was used for the studies. First, the spindle was dipped into the nanogel till the notch on the spindle touched the nanogel surface¹⁵.

h) Extract content: For the estimation of the extract in nanogel, extract was extracted from 1 gm of nanogel formulation with 50 ml of phosphate buffer 6.8 and mixture was filtered through membrane filter (pore size 0.45 µm). From this, 2 ml was pipette out and made upto 10 ml. The absorbance of the sample was determined spectrophotometrically at 276 nm. The concentration of extract was estimated from the calibration curve¹⁶.

i) In vitro Release studies: The drug release from the formulation was determined by using the apparatus known as Franz Diffusion Cell, which consist of a cylindrical glass tube which was

opened at both the ends. 1 gm of nanogel equivalent to 10 mg of extract was spread uniformly on the surface of cellulose nitrate membrane (previously soaked in medium for 24 hrs) and was fixed to the one end of tube. The whole assembly was fixed in such a way that the lower end of tube containing nanogel was just touches (1-2 mm deep) the surface of diffusion medium i.e. 100 ml of pH 6.8 phosphate buffer contained in 100 ml beaker. The assembly was placed on thermostatic hot plate with magnetic stirrer and maintained at temperature 37°C ± 2°C, the contents were stirred using magnetic bar at 100 rpm for a period of 24 hrs, 1 ml of samples were withdrawn at different time intervals. This 1ml was diluted upto 10 ml of fresh phosphate buffer (pH 6.8) and sample were analyze at suitable nm in UV-Visible spectrometer for extract^{17,18}.

j) Skin irritation test:

No irritation -0

Slight irritation -1

Irritation -2

Test for irritation was performed on human volunteers. For each nanogel, 12 volunteers were selected and 1.0 g of formulated nanogel was applied on an area of 2 square inch to the back of hand. The volunteers were observed for lesions or irritation.

k) Microbial Assay: All the nanogel formulations were assayed for their antibacterial activity against gram positive (staphylococcus aureus) and gram negative (Escherichia coli). the assay was carried out by cup and plate method. Zone of inhibition indicates the formulation that give better effect to cure antimicrobial activity¹⁹.

l) Stability: Batches evaluation the stability studies were carried out on optimized formulation. The



samples were stored at $40^{\circ}\text{C} \pm 2^{\circ}\text{C}$ and $75\% \pm 5\%$ relative humidity for three months as per ICH guidelines. After 1, 2 and 3 months samples were withdrawn and tested for appearance, pH, particle size, drug content, spreadability, extrudability, viscosity²⁰.

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