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Gold Nanoparticles for Skin Drug Delivery System

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Abstract: *Gold nanoparticles (Au NPS) are becoming an effective Nano carrier for targeted and controlled drug delivery through the skin. Their special properties-such as very small size, high surface area, adjustable chemistry, and good Biocompatibility – help them pass through the skin barrier quickly and keep drugs at the target area for a longer time.*

Au NPs can also be combined with different medicines, peptides, or ligands to improve how well they work and to reduce side effects. Their optical and heat- based properties also make them useful for both treatment and diagnosis in skin –related therapies.

This review explains how gold Nano particles are made, analyses, and modified, as well as how they penetrated the skin and their potential use in treating conditions like skin cancer, infections, and inflammatory diseases, although they have many advantages, challenges like toxicity, large- scale Production, and regulatory approval must be solved before they can be widely used.

Overall, gold Nanoparticles show promise as effective tools for future skin drug- delivery systems.

Keywords*:* Gold Nano particles (Au NPs), Skin drug delivery, Nano carriers, Biocompatibility, penetration enhancement Skin permeation, Characterization

I. INTRODUCTION

Transdermal delivery system (TDS) or transdermal therapeutics system (TTS) or skin-applied formulations that allow medicines to enter the body and produce effects throughout the whole system. When a medicine passes through intact (unbroken) skin and reaches the bloodstream in helpful amount, it is called transdermal drug delivery. [1]

Since the 19th century, the medical field has grown rapidly. Dr. peter paul species is known for creating nanoparticles. [2] the word Nano comes from the Latin word Nanos meaning "very small", and this Greek origin also refers to something tiny. Nanotechnology involves designing, creating, and using extremely small system, devices, and structures by changing their size and shape at the level of nanoparticles. [3]

Gold nanoparticles (Au NPs) are important because they have unique physical and chemical properties.

- They are chemically stable and non-toxic.
- They are easy to produce, and their size usually ranges from 1 to 150nm.
- Due to their shapes and sizes, Au NPs can effectively carry drugs and allow controlled release in different ways. [4]

Delivering medicines through the skin is a very effective method. The transdermal drug delivery system (TDDS)is a new and useful approach in the pharmaceutical field because it has several advantages over traditional methods.

conventional system often need higher doses and long-term use, which may lead to side effect and poor patient compliance. [5]

nanoparticles are now widely studied due to increased awareness of their effect on human health and the environment, [6] as well as the rising number of man- made nanoparticles released around us. All health professionals should understand basic skin structure and function because the skin is also called the cutaneous membrane. [7]

Nanoparticles (NPs) are used as carriers for drugs and diagnostics agents. these include polymeric, NPs, micelles, Nano capsules, liposomes, and solid nanoparticles. [8] Gold nanoparticles, in particular, have many medical uses because of their good conductivity, low toxicity, high surface-to-volume ratio, and strong biocompatibility.

In water-based solutions, Au NPs show a wide range of colors due to their size and their absorption peak between 500 and 550nm. [9]

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Nanoparticles and Nano pharmaceuticals come in many types, including organic, inorganic, lipid-based, polymeric, and Nano capsules. [10]

According to the FDA, drugs are substances used to diagnose, cure, treat, or prevent disease, and also used to effect the structure of function of the body. Drugs are expected to reach disease- causing cells in extract amount to be effective Way. [11]

CLASSIFICATION OF NANOPARTICLES- [12-14]

1. Organic nanoparticles
2. Inorganic nanoparticles
3. Carbon based nanoparticles

TYPES OF NANOPARTICLES: - [15-16]

Types of Nanoparticles are as follows: -

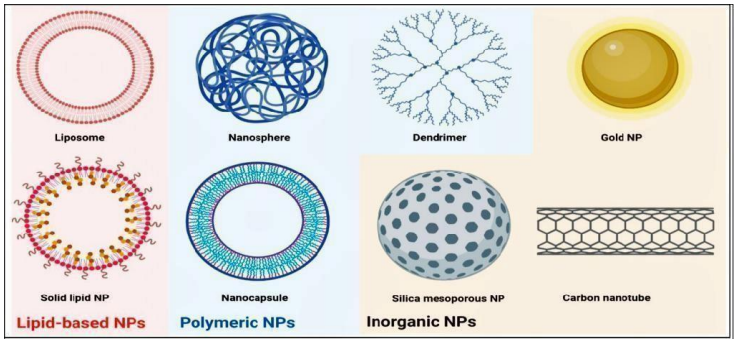

Fig.1: - General structure of the most common Synthetic nanoparticles use for drug delivery [17]

Nano Carriers improve drug delivery by allowing for better targeting, controlled release, and bioavailability. Here are the primary types. [16]

Nano-carriers help improve drug delivery by providing: -

- Better targeting
- Controlled drug release
- Improved Bioavailability

1. Organic Nanoparticles: -

This section describes the advantages and disadvantages of organic nanoparticles such as carbon nanotubes, quantum dots, dendrimers, liposomes, and polymers.

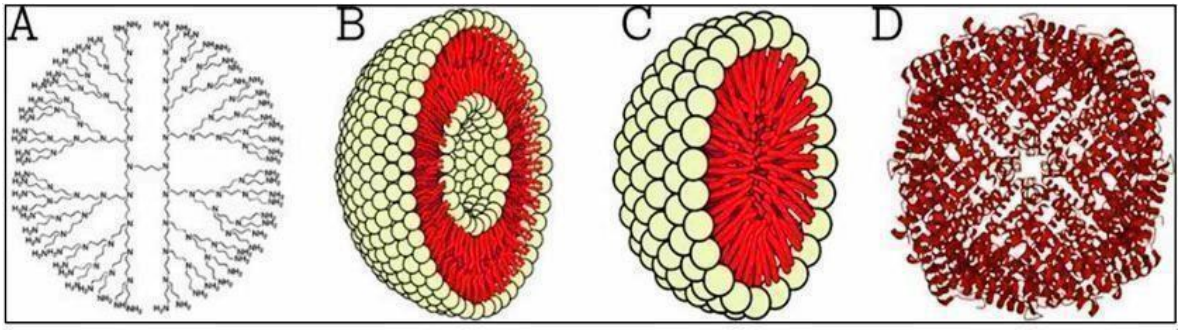

Fig. 2- Types of organic Naps [19-21]

a) Dendrimers
b) Liposomes
c) Miscalls

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d) Ferritin

A) Dendrimers-

Dendrimers are highly organized, branched macromolecules that look like trees. Because of their many branches, they have a large surface area that can bind medicines.

This makes them useful for carrying different therapeutics agents or targeting ligands. [12-22]

The word dendrimer comes from a Greek word Dendron, which means "tree " [23] which accurately describes their branched structures. [24]

B) Liposomes-

Liposomes are single-layer or double-layer structures are made of phospholipids arranges themselves so that a liquid core becomes enclosed by the bilayers. Since the 1970s, phospholipids have been used to carry drugs as micro-or nanoparticles for delivering medications.

Liposomes are spherical vesicles created from the Greek words lips(fat)and soma (body). They are made of phospholipid molecules shaped into a circular sac. inside this sac is a water droplet that is designed to carry drugs across the cell membrane. Liposomes are typically about 1000 nm is size. [17]

They are used in many areas of drug delivery, including both dermal and transdermal application. For skin delivery, liposomes help enhance drug penetration and localize drug action while minimizing an absorption into the bloodstream. [26]

Types of Liposome [27]

1. Traditional Liposome:

contain a single phospholipid bilayer.

2. Long- circulating Liposome:

Formulated with additional polymers, such as PEG, to increase their time in circulation.

3. Cationic Liposomes:

positively charged lipids are added to the bilayer to improve gene delivery.

4. Targeted Liposomes:

Designed to reach specific cells or organs by attaching targeting ligands to the phospholipid ligands to the phospholipid bilayer.

Composition of liposomes

Liposome are among the most studied Nano carriers for antimicrobial drug delivery. Their size ranges from 0.02 to 10 um and they consist of phospholipid bilayers surrounding an inner aqueous compartment. Liposomal drug formulation is widely used in nano medicine, with more than fifteen FDA-approved liposomal drugs currently available. [28]

c) Micelles-

Micelles are colloidal structure that form when amphiphilic molecules self-assemble in water at concentration above their critical micelle concentration (CMC). [29]

POLYMERIC NANOPARTICLES

Polymeric nanoparticles are biodegradable particles made from polymers such as poly (lactic- co-glycolic acid). They are commonly used for controlled drug released and are biocompatible, making them suitable for sustained-releases therapies. [22] Because they break down naturally and are safe for the body, polymeric nanoparticles can increase drug bioavailable while reducing toxicity.

Polymeric nanoparticles are generally classified into three types:

• Hydrogels
• Nano spheres
• Nano capsules, which include polymeric micelles and polymerase.

These can be made from natural or synthesis polymers, most of which are biodegradable and biocompatible. [17]

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2. Carbon-based Nanomaterials

Examples include fullerenes, carbon nanotubes, and graphene. These materials have unique physical and chemical properties that make them useful in drug delivery, diagnostics, and tissue engineering. [12] carbon nanotubes and graphene oxide have large surface areas and the can be functionalized for various biomedical application. [30]

3. Inorganic nanoparticles

Inorganic nanoparticles include metal, ceramic, magnetic, and nano shell structures. They differ in size, properties, advantages, and uses.

Inorganic nanoparticles are generally much smaller than organic nanoparticles, typically reengining from 1-100 nm, and can carry drug most efficiently. [18]

Common types include:

I. Metal Nanoparticles Ex: -gold, silver

II. metal oxide nanoparticles Ex:-Iron oxide

They are widely used in imaging targeted drug delivery, and cancer therapy-particularly in photo thermal and photodynamic treatments.

I. Metal nanoparticles-

Metal nanoparticles are mainly of two types:

- 1.Gold nanoparticles (Au NPs)
- Silver nanoparticles

I. Gold nanoparticles-

Gold nanoparticles are among the most widely used nanomaterials in research and medicine. They are popular because of their:

- excellent physicochemical stability
- low toxicity
- minimal enzyme degradation
- good electrical and chemical properties [31]
- Gold nanoparticles have a multiple therapeutic application.
- . they can be used for:

Targeted delivery of vaccines, nucleic acids (DNA/RNA), AND Antibodies, cancer therapy, [29] therganostic application (combined therapy diagnostics)

When carrying DNA or RNA, gold nanoparticles help protect nucleic acids from degradation and assist in delivering them to the cell nucleus.

They are also used in tissue regeneration and various biomedical fields. [32]

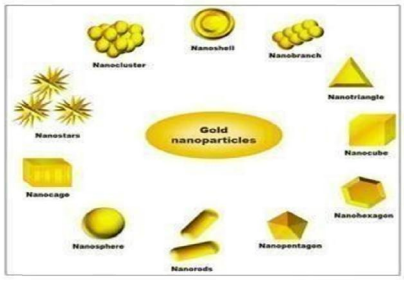

Fig. 3- Different shapes available for nanoparticles. [31]

- Preparation of gold nanoparticles

Gold nanoparticles can be made using several methods. one common method is the Turkevich and ferns method:

- mix chloroauric acid and trisodium citrated.
- Heat the solution while stirring for about 30 minutes.

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After cooling, gold nanoparticles form and appear yellow to burgundy in color. The color change shown that the nanoparticles have been formed correctly. [31]

 AuNps and Cytotoxicity

Before using gold nanoparticles in medicine, it is important to study their toxicity. Their toxicity depends on factor like:

 size of particles
 surface charge
 chemical groups on the surface
 Determining particles Size

The size of nanoparticles can be measured using special instruments such as:

 Particles Size Analyzer (Horiba SZ-100)
 Dynamic Light Scattering (DLS)

These tools help measure nanoparticles in water at room temperature for testing. [4]

Determination of particle size of Nanoparticles

The particle size of the nanoparticles was measured using particle size Analyzer 9 (Horiba SZ- 100) and the dynamic light scattering (DLS) Method.

The nano emulsion samples were mixed in water and started at room temperature. All measurements were taken at a scattering angle of 90. [33]

CHEMICAL PROPERTIES OF GOLD NANOPARTICLES TO SKIN DRUG DELIVERY-

• Biocompatibility of AuNPs:- Gold nanoparticles (Au NPs) depends on how they behave inside the body. This can have studied by examining:

o pharmacokinetics (how the body processes them)
o Tissue distribution (where they travel in the body)
o toxicity
o clearance (how they are removed from the body) [34]

• Targeting

Gold nanoparticles can target specific tissues in two ways: -

1. Passive Targeting

This occurs because of enhanced
permeability and retention (EPR) effect. some tissues, like tumors, have leaky blood vessels that allow nanoparticles to enter more easily.

2. Active Targeting

In this method, gold nanoparticles are modified so they can bind to specific cells, such as tumor cells. They may respond to external or internal stimuli to improve drug delivery. [34]

CHARACTERISTICS OF NANOARTICLES- [35]

Nanoparticles can be studied using different methods, including:

 UV-Visible spectroscopy
 X-ray diffraction (XRD)
 Electron microscopy
 mass spectrometry

ANATOMY AND PHYSIOLOGY OF SKIN-

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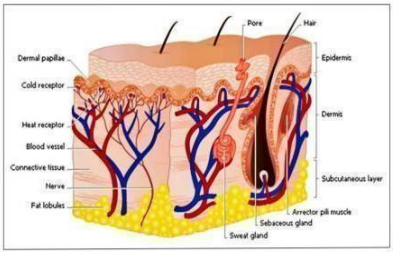

Fig.4- Structure of human Skin [36-37]

The skin acts as a very effective barrier. it prevents excessive water for the body and block harmful substance (xenobiotic) from entering. this protection helps us survive different environment condition.

most substances pass very slowly through the stratum carenum, which is the outermost layer of the skin. The stratum carenum prevents drugs from entering the skin quickly because it has:

- High density (1.4g/cm in dry state)
- Low moisture (15-20%)

Because of this, only a few drugs can easily pass through the skin.

The stratum carenum is constantly renewing, which further limits how much medicine can be absorbed through the skin. [36]

Over time, transdermal delivery system has evolved through three generations:

1. First generation: -Traditional patches that deliver drugs able to cross the skin naturally.
2. Second generation: -systems designed to increase skin permeability and improve drug delivery. [38]
3. Third generation: -Advanced methods targeting deeper layers without damaging the skin. The epidermis (outer skin layer) consists of five sublayers, from outside to inside:

o Stratum carenum
o Stratum lucidum
o Stratum granulosum
o Stratum spinosum
o Stratum Basale

Each layer has different types of keratinocytes (skin cells). [39]

TYPES OF SKIN – [40]

- Normal skin
- Dry skin
- Oily skin
- Combination skin
- Sensitive Skin

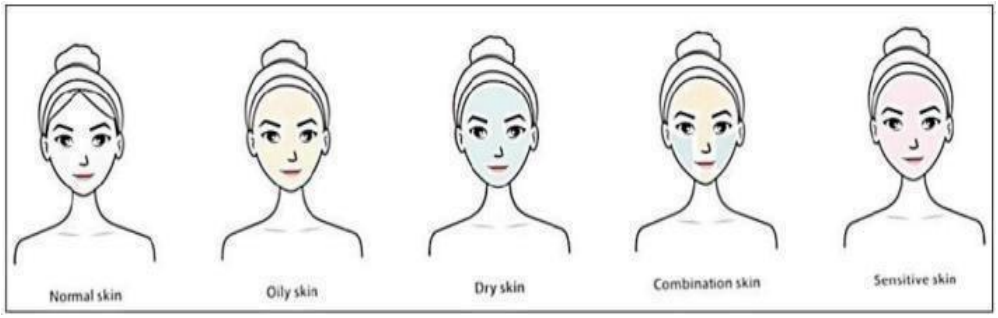

Fig. 5- Illustrates several skin types based on moisture level and lipid content [41]

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SKIN TYPES AND THEIR CARE: -

The skin divided into 4 major groups. Each group needs specific ingredients to help Keep the skin healthy and functioning properly. [42]

Skin type	Features	Herbs	Essential oil
Oily Skin	1. Shiny and often has breakouts. 2. Coarsepores and pimples.	Aloe Vera, Thyme, Lemon Grass	Bergamot, Lavender, Juniper
Dry skin	A feeling of skin tightness. Fine lines.	Aloe Vera olive oil, calendula	Chamomile Fennel Geranium, Lavender
Combination skin	Oilyskin on the forehead, shine, Blackheads. 2. Dullness and fine lines on cheeks	Witch hazel, menthol, Aloe Vera, Turmeric	Citrus oils, jasmine oil, Sandal wood oil
Normal skin	1. Neither oily nor dry 2. Appears smooth	Pomegranate, Herbal face pack, Gingili oil	Chamomile Fennel, Geranium, Lavender, Sandal wood

Table 1- Skin type and their care

These types are identified based on the skin's moisture level and oil (lipid) content.

GOLD NANOPARTICLES FOR SKIN DRUG DELIVERY SYSTEM

 Layers of the skin -

The skin is the largest organ of the body. its surface area ranges area ranges from 1.7 to 2.0 square meters. [42]

It has three main layers: [43]

1. Epidermis (outer layer)
2. Dermis (middle layer)
3. Hypodermis (inner layer or subcutaneous tissue)

1. Epidermis-

• The epidermis is a multilayered outer covering of the skin.
• Its thickness changes depending on the body part.
• palms and soles: about 0.8mm
• Eyelids: about 0.06 mm

It includes the stratum carenum (outer part) and the viable epidermis.

[44] It has four layers;

o Stratum Basal
o Stratum spinosum
o Stratum granulosum
o Stratum corneum

Keratinocytes in this layer produce protective substances like keratin and lipids that help form the skin's barrier. [45]

2. Dermis-

• The dermis is 3-5 mm thick and made of connective tissues.
• It contains blood vessels, lymph vessels, and nerves.
• It supplies the skin with nutrients and oxygen and remove waste.
• It also includes hair follicles, sweat glands, oil gland, and immune cells. [37]

3. Hypodermis

• Also known as subcutaneous fat tissue.

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• Supports the dermis and epidermis.
• Stores fat, helps regulate body temperature, and provides protections.
• Contains major blood vessels and nerves.
• the skin and may contains sensory pressure organization. [44]

MECHANISM OF SKIN PENETRATION-

 Penetration of Drugs into the skin -

Many medicine are given through the skin (Trans dermally) so they can reach deferent layers such as the dermis, subcutaneous tissue, and muscle. for these drugs, it is important to know how much of the drug reaches different skin levels and how it behavers once it enters. This helps in measuring how much of the drug becomes available in the body and in comparing different drug formulations. [46]

 Follicular Penetration: (Shape- Dependent study)

Gold nanoparticles (GNPs) of different shapes were tasted on human skin samples. All particles were the same overall size (100nm), but their shapes different- rod shaped, spherical, and star- shaped.
Gold Nano rods- showed good penetration and were mostly found in sebaceous glands.
Gold nano Stars-Showed the highest penetration of all shapes.
Gold spheres- Could enter the glands, but also accumulated in various skin areas. [47]

DRUG DELIVERY APPORACHES FOR SKIN DISEASES

Gold nanoparticles are extremely small and can enter the skin easily and safely, with very low toxicity and without causing injury. Because of this, they are commonly used in Nano carrier formulations for treating skin disorders. Using nanoparticles for cutaneous (skin) treatments is preferred because they have fewer side effects. Typical creams, gels, and ointments often do not for effective drug delivery, unlike Nano carriers. [48]

NANOCARRIERS AS EFFECTIVENE DIAGNOSIS AND TREATMENT FOR THE SKIN CANCER -

Nano carrier- based systems have unique chemical and physical properties, allowing them to be used as tools for diagnosis. they can help detected and monitor tumors, giving cancer patients better hope.
Nanoparticles also:
• Improve drug pharmacokinetics
• Increase bioavailability
• Reduce immunogenicity
• Extend half – life
• Reducing immunogenicity
Increases solubility of drug that do not dissolve well in water Allow multiple drugs to be given together Enable controlled release of therapeutic molecules. [49]

FUNCTIONS OF THE SKIN

 Acts as protective barrier against
 mechanical, thermal, and physical injury, as well as harmful substances.
 prevents moisture loss, helping maintain skin hydration.
 Reduces harmful effects of UV radiation from the sun. [50]

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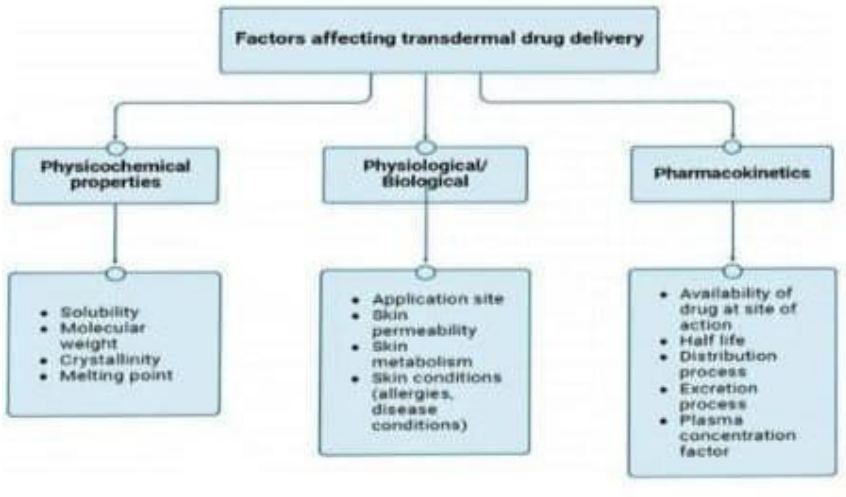

Fig.6: General factors responsible for transdermal system [51]

ADVANTAGE OF NANOPARTICLES

1. Reduced side effects: -

Nono spong used in drug delivery system reduce the risk of unwanted side effect by ensuring that only a minimal amount of the drug comes into contact with healthy tissues. [2]

2. Better formulation properties: -

Nanoparticles improve the flexibility, appearance, and stability of drug formulations. they are biodegradable, non-toxic, site- specific, and can be stored for more than a year. [52]

3. Deep tissue penetration: -

Nanoparticles can pass through tissues and even reach very small capillary vessels. they can move through the skin using transcellular or par acellular pathways. [53]

4. Multiple administration routes:

Nanoparticles can be given orally, nasally, by injection (parenteral), or even through the eye (intra-ocular). [25]

DISADVANTAGES OF NANOPAERTICLES

1. Storage problem:

Liposome can become unstable during storage causing dumping, causing clumping, leakage, or changes in size and structure. [54]

2. Large particle proportion:

Some particles may still be in the micrometer range. [53]

3. High reactivity:

Because nanoparticles are very small and have a large surface area, they react easily in biological environment. [12]

4. Dose dumping risk:

In Nano sponges, the cross linker may dissolve too quickly, causing a sudden release of the drug. [2]

APPLICATION IN SKIN DRUG DELIVERY

• Gold Nanoparticles: - Can be encapsulation in lipids and used in drug delivery. [55]

• Nanoparticles in gene therapy: - They are also used to deliver genes and help replace defective genes involved in cancer, viral infection, and other genetic diseases. [8]

• Lipid- polymer hybrid nanoparticles: - These are used for removing microbubbles using ultrasound and have shown god results in treating cancer, viral infection, and genetic disorder. [8]

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• These hybrid nanoparticles are also used to remove microbubbles using ultrasound. [55]

APPROACHES OF TRANSDERMAL DRUG DELIVERY SYSTEM-

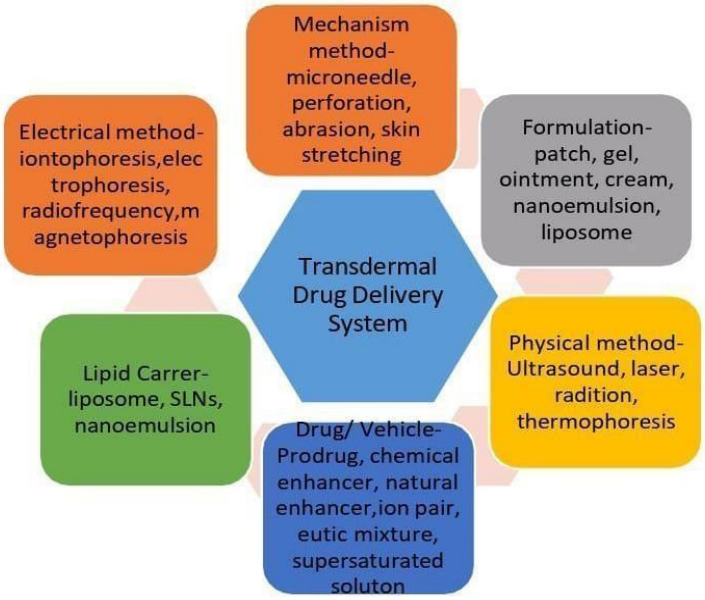

Fig .7: - A scheme representing the approaches for the development of transdermal drugs delivery system. [25]

II. CONCLUSION

Gold nanoparticles (Au NPs) are a highly promising option for skin drug delivery because they are: -

• Excellent Biocompatible
• Adjustable in size
• Easy to modify on the surface
• Able to penetrate the skin barrier effectively.

Their unique physical and chemical properties help: -

• Controlled and targeted drug delivery
• Improved drug stability
• Better bioavailability
• Reduced side effects.

Au NPs can also be customized for various medical applications.

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