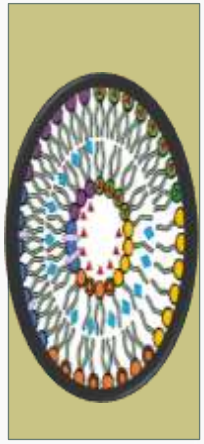
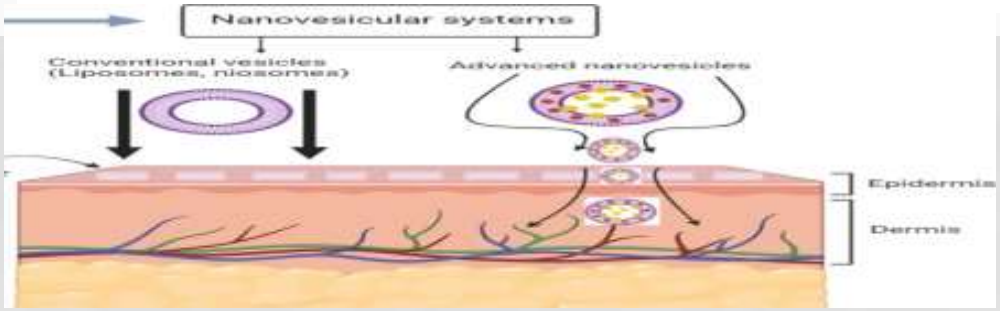
كلية الصيدلة – جامعة بغداد

تقييم وحدة الشؤون العلمية

الورشة الموسومة:

The Evolution of Emerging Nanovesicle Technologies for Enhanced Delivery of Molecules into and across the Skin





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- الثلاثاء ٢٥/ ٢٠٢٥/٢

-قاعة الكندي في فرع الصيدلانيات

-الساعة ١١:٣٠ صباحا

Topical administration of pharmaceutical and cosmeceutical agents

- ✓ **Dermal delivery** to treat skin disease (target to various skin region)
- ✓ **Transdemal delivery** (for systematic effect)

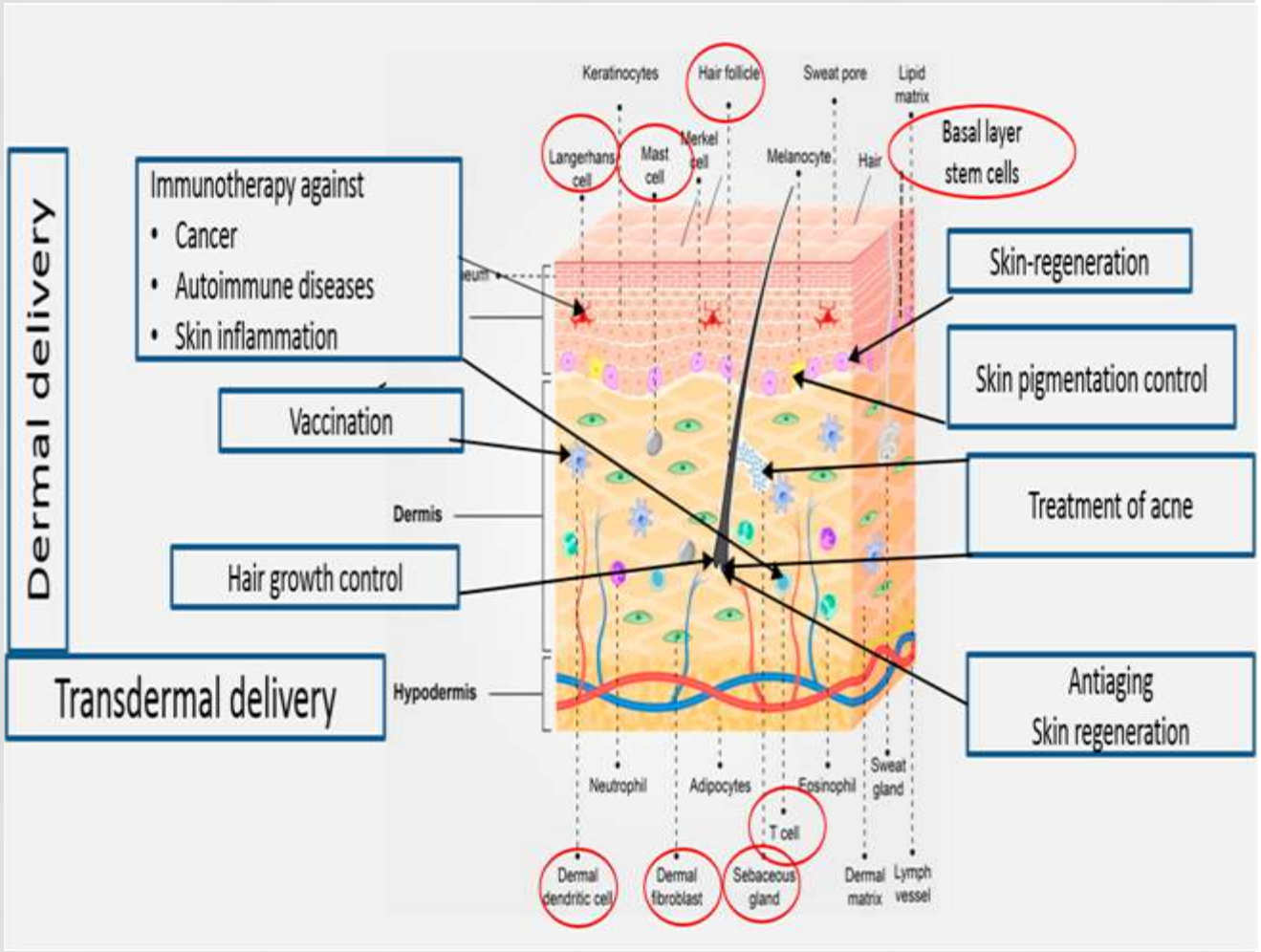


Figure : Treatments targeting cellular elements in the skin

Generally, the acceptability of **topical and transdermal products** is **extremely high**, which is also evident from **the growing market** for these products.

This is demonstrated by the fact that the value of skin delivery, which was estimated to be approximately **$12.838 billion in 2020, is anticipated to rise to $13.457 billion by 2026** with a compound annual growth rate higher than that of other delivery routes

Table: A non-exhaustive list of marketed transdermal systems

Drug	Year	Application(s)	Example of commercially Available product(s)	Penetration enhancement effect and penetration Enhancers
Scopolamin	1979	Motion sickness	Transderm Scop	Occlusive effect
Nitroglycerin	1981	Angina pectoris	Nitro-Dur, Nitrodisc, Transderm-Nitro	Occlusive effect, fatty acid esters
Clonidine	1984	Hypertension	Catapres TTS	Occlusive effect
Fentanyl	1990	Moderate to severe chronic pain	Duragesic	Occlusive effect
Nicotine	1991	Smoking cessation	Nicoderm CQ, Prostep, Habitrol	Occlusive effect
Lidocaine/Prilocaine	1992	Anesthesia	EMLA Anesthetic Disc	Occlusive effect, polyoxyethylene fatty acid esters
Testosterone	1993	Hormone replacement therapy in hypogonadism	Androderm	Occlusive effect, glycerol monooleate
Estradiol/norethisterone Acetate	1998	Hormone replacement therapy for menopausal symptoms	Combipatch	Occlusive effect, silicone, oleic acid, dipropylene glycol
Lidocaine	1999	Anesthesia for post-herpertic neuralgia pain	Lidoderm	Occlusive effect, urea, propylene glycol
Oxybutynin	2003	urinary incontinence	Oxytrol	Occlusive effect
Methyphenidate	2006	Attention deficit hyperactive disorder	Daytrana	Occlusive effect
Buprenorphine	2010	Chronic pain	Butrans	Occlusive effect

Pathways for Skin Penetration

The three possible routes of penetration of a compound applied topically through the skin are well known:

(i) the hair follicle route
(ii) the intracellular route (transcellular)
(iii) the intercellular route (provides a **significant barrier** to skin permeation)

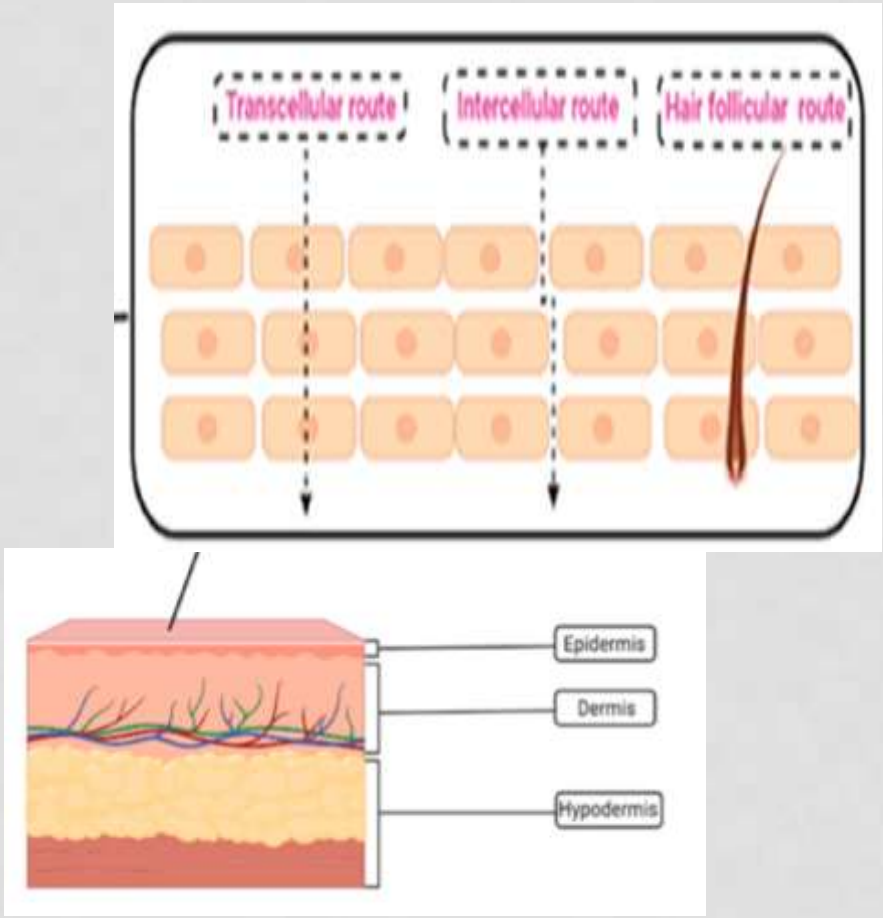
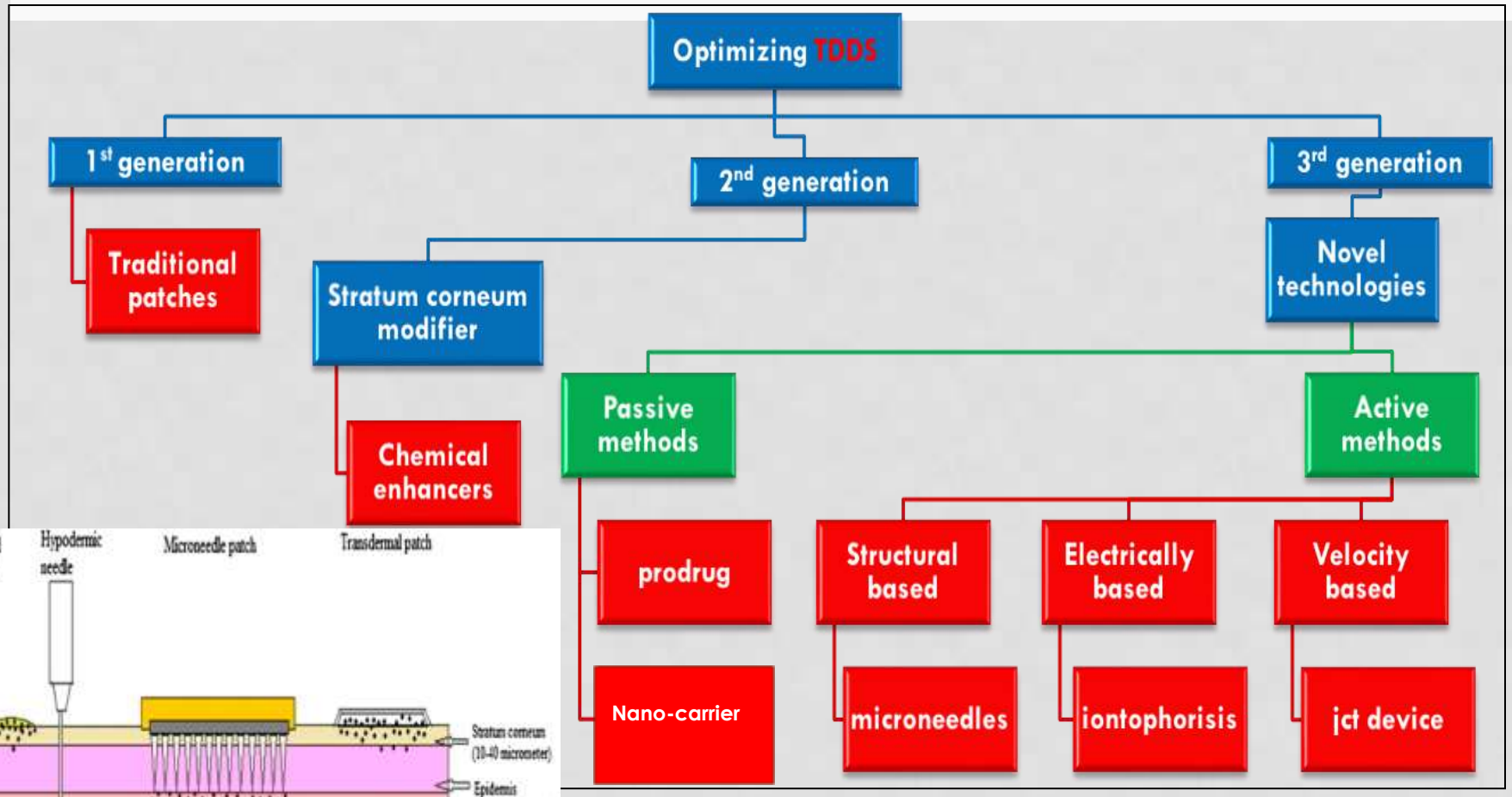


Figure: The skin anatomy and how it relates to the routes of skin penetration

Strategies for enhancement drug permeability through stratum corneum



Classification of Lipid Nanosystems

Lipid- nanocarrier:

- Ease drug penetration through skin
- Provide controlled/ modified drug release
- Occulsive effect on skin
- Non-irritant and non toxic properties
- Safe to use on damaged or inflamed skin

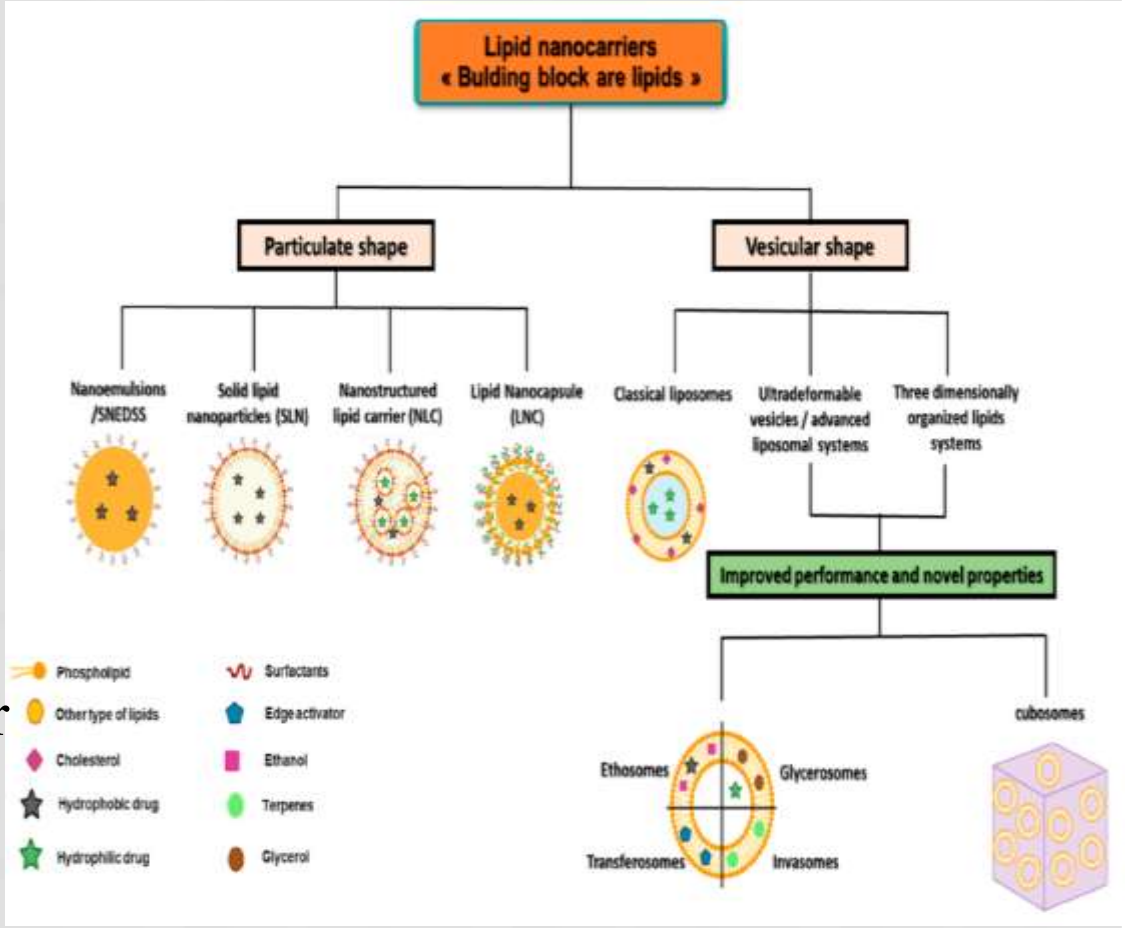


Figure 2. Classification of the main types of lipidic nanosystems for dermal and transdermal drug delivery.

Vesicular Carrier Systems: Conventional and advanced Liposomes

Liposomes are spherical vesicular lipid-based nanocarriers consisting of **phospholipid** and **cholesteral.**

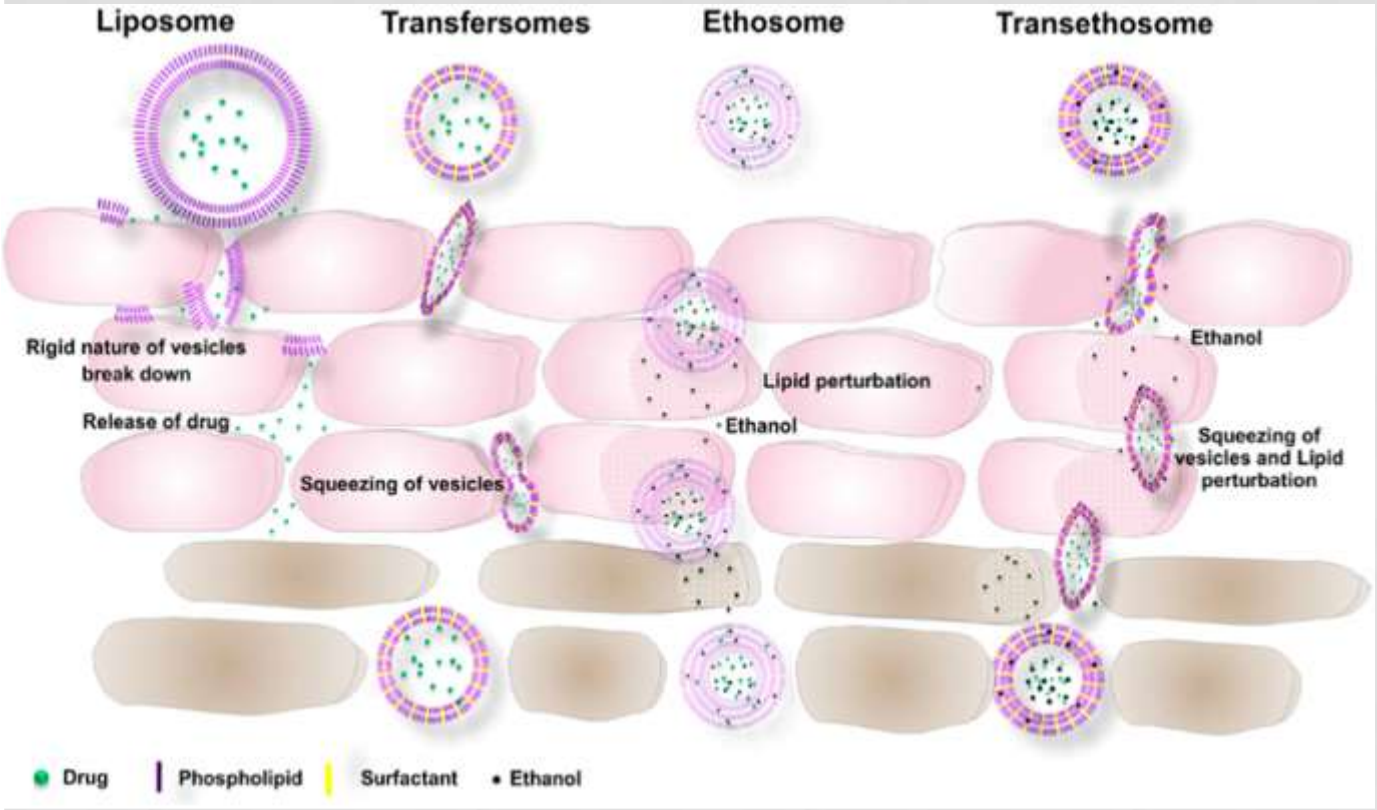


Figure: Mechanism of some vesicular nanocarriers across the stratum corneum

The most commonly observed mechanism Involve: **deformation**, **alteration of intercellular** domains and **increased flexibility**

Factors Affecting Skin Penetration of Nanovesicles: Size

- In general, **smaller particle size** has **a positive effect** on the **transdermal penetration** of a drug encapsulated into lipid nanosystems
- nanosystems with **a diameter of 600 nm or greater** are unable to deliver encapsulated drugs to deeper skin layers.

- Nanovesicles with **a diameter of 300 nm** or less could deliver their content **into the deep layers** of the skin and penetrate preferentially via the transfollicular route

- Nanosystems with **a diameter of 100 nm or less** are suitable for deep skin penetration and allow the onset of action .

Factors Affecting Skin Penetration of Nanovesicles: Size

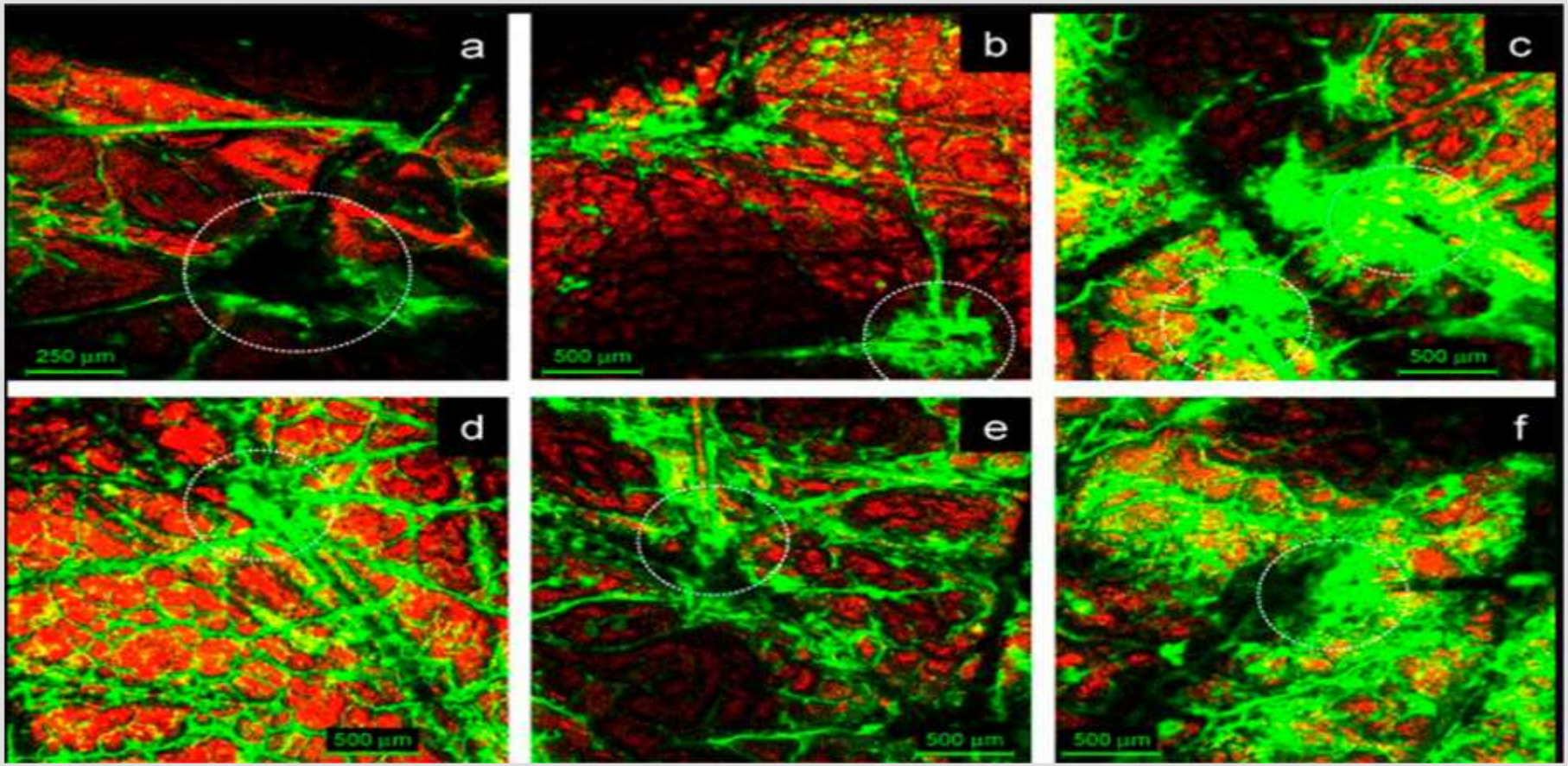


Figure:. x-y images of the follicular localisation of fluorescent nanoparticles after application of nanoparticles **(20 nm) for (a) 30 min, (b) 1 h and (c) 2 h** and of nanoparticles **(200 nm) for (d) 30 min, (e) 1 h and (f) 2 h**. Hair follicles are represented by white circles.

Factors Affecting Skin Penetration of Nanovesicles: Shape

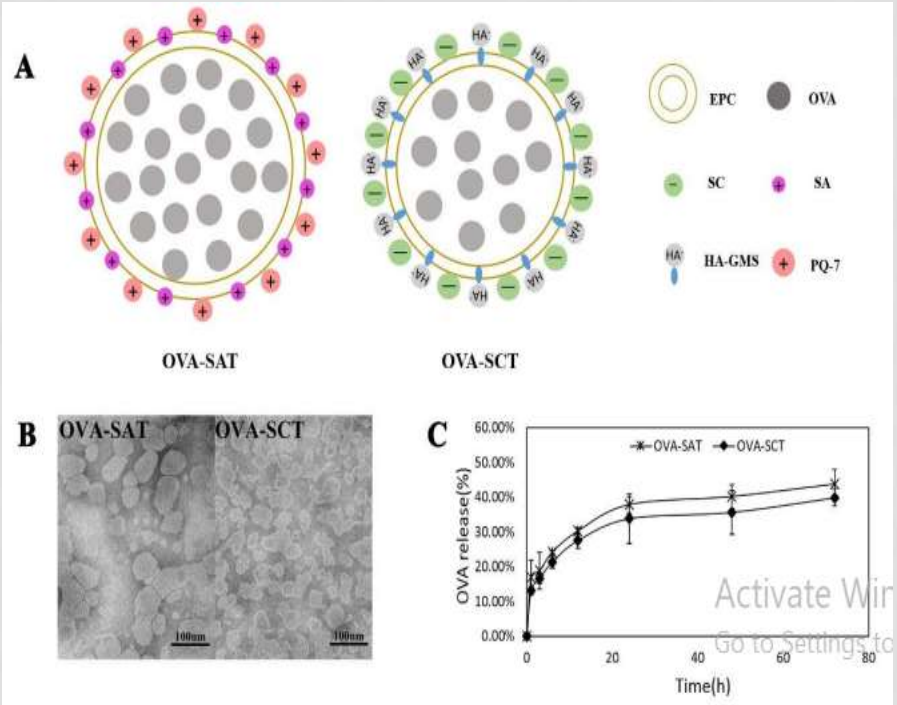
The nature of the interaction between a nanovesicles and a lipid bilayer is highly influenced by the particle's **shape**, **volume**, **local curvature** at the point of contact, and **initial orientation**. This will directly impact their capacity to permeate the lipid bilayer.

Mathematical studies show that, depending on how it hits the membrane, **an ellipsoid particle** can go through a lipid bilayer up to five times faster if it hits it in a certain way.

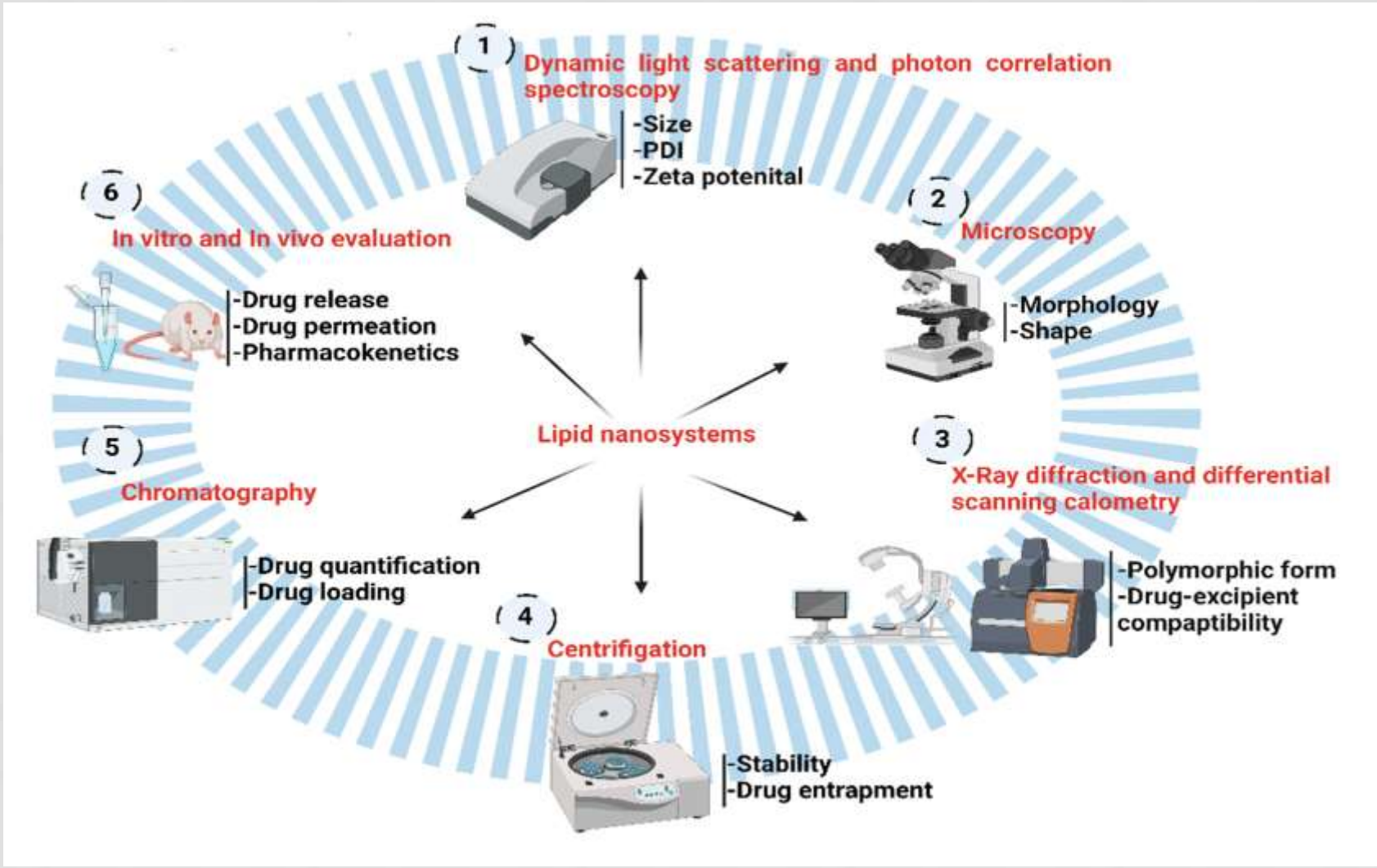
Factors Affecting Skin Penetration of Nanovesicles: surface charge

-The presence of charge could enhance skin adhesion and the interaction of nanosystems, leading to a higher therapeutic effect on inflamed skin

Antigens have been encapsulated in transferosomes with opposite surface charges and inserted into dissolving microneedles for transdermal immunisation. The results showed that cationic nanovaccines can escape endocytic compartments,allowing antigen processing via an MHC-I presentation pathway and increasing lymph node accumulation



Common characterization and evaluation techniques of nanovesiceles



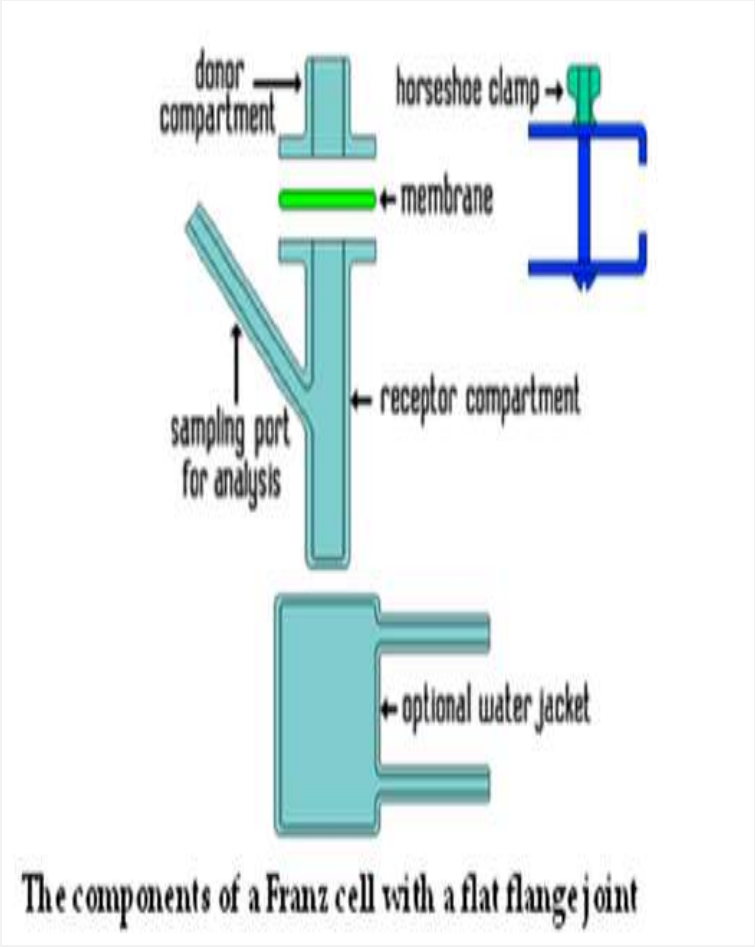
In vitro methods use rapid and cost-effective assessments of drug permeation through synthetic or biological membranes.

Franz diffusion cell

The flux and apparent permeability are calculated by using the following Equation:

Permeability (Papp) = Flux/Cd

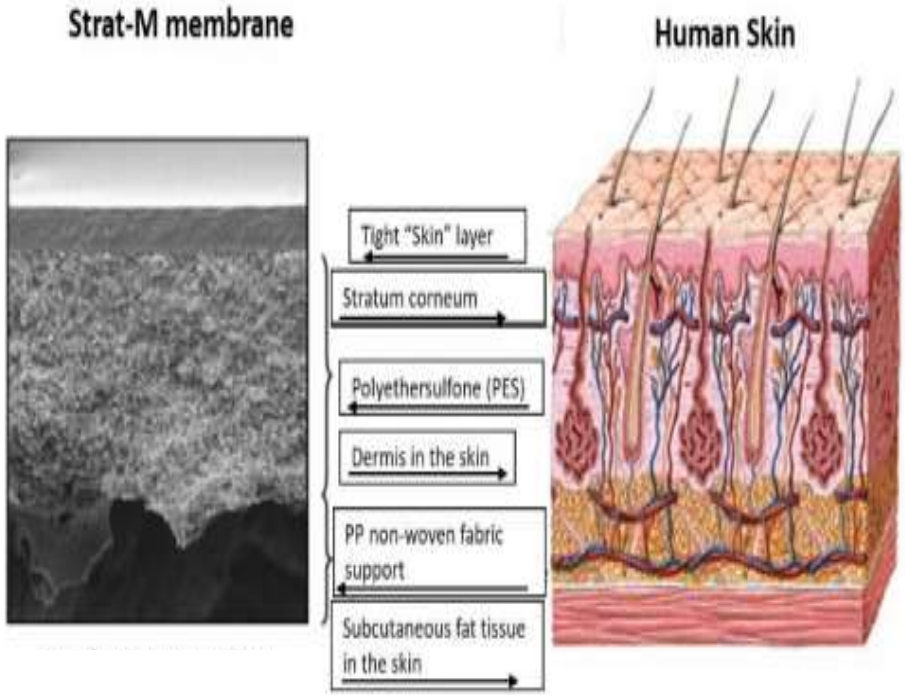
Flux (J) was calculated by dividing the slope obtained by plotting the cumulative amount of drug permeated (M) through the skin vs. time (t) with the cross-sectional area of the membrane (A) exposed to the drug. Cd was the initial drug concentration in the donor chamber



The components of a Franz cell with a flat flange joint

Synthetical membranes are designed to mimic the human skin and offer:

- ✓ a **simple and reproducible** alternative to human and animal skins.
- ✓ can be **easily procured and stored**.
- ✓ They also **reduce the variability** in drug permeations that is associated with the utilization of biological skin
- ✓ Ethical concerns



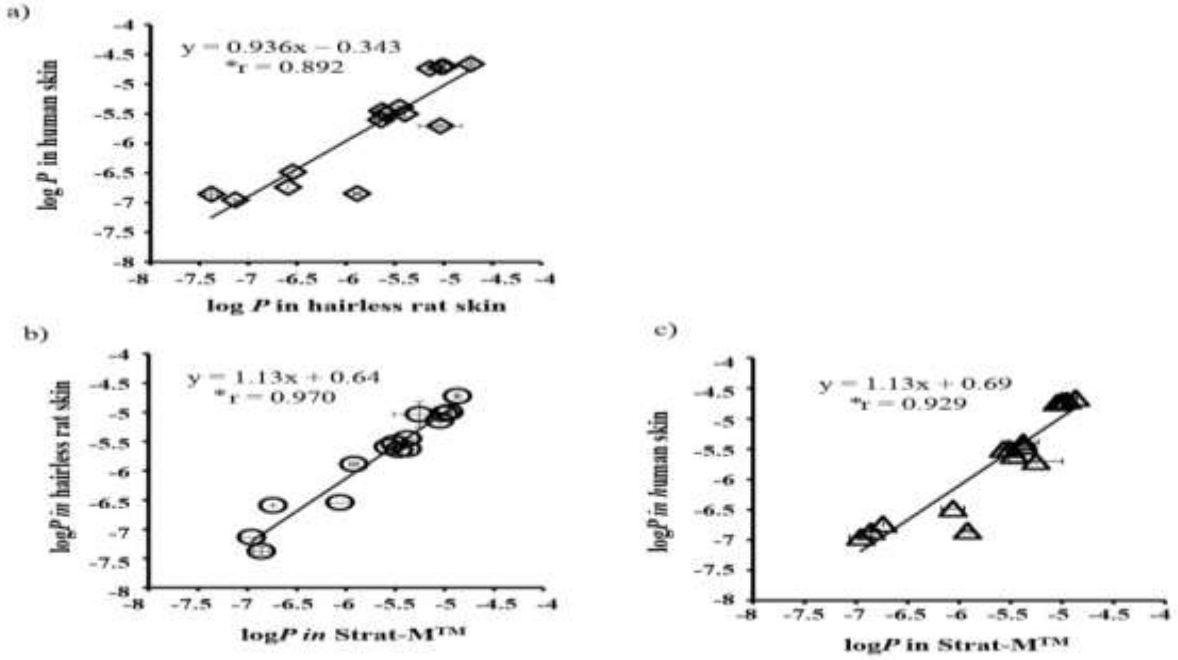


Figure: Relationships between log P values of human skin and rat skin or Strat-M™. (a) Human skinvs. Rat skin, (b) Rat skin vs. Strat-M™, (c) Human skin vs. Strat-M™.

In vivo models provide a more accurate estimate of the amount of drug absorbed through the skin.

- **Ex Vivo Methods**

These methods included:

- T***ape stripping method*** (the stratum corneum is removed by repeatedly applying tape to the surface of the skin, which causes the tape to partially remove the skin barrier.

- **Confocal lasery microscopy** to track drug transit through transdermal route

Conclusion

- The utilisation of lipid nanovesicles in dermal and transdermal applications is widely regarded as the next frontier in the treatment of topical and systemic diseases due to the ability of the nanomaterials to achieve desirable spatiotemporal delivery of payload.
- Despite the many successes of lipid nanosystems in dermal and transdermal applications, it remains to be seen whether their utilisation will ultimately improve the treatment outcomes of many diseases in the present and future diseases

Thank you
Any
question?