



# Permeation enhancers: excipients to be considered in topical formulations with systemic adverse effects

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## Background

Most topical dermatologic preparations are presented as semisolids meant to be locally active. Although the stratum corneum acts as the rate-limiting barrier, variable systemic adverse effects may occur due to drug permeation through the skin (1). Formulations often include penetration enhancers either intentionally selected for this function or as excipients with other purposes which end up by facilitating the percutaneous absorption of the active ingredients.

## Results

Occlusive dosage forms, such as ointments, may promote drug permeation by increasing the hydration and temperature of the stratum corneum. Concerning excipients several mechanisms have been identified:

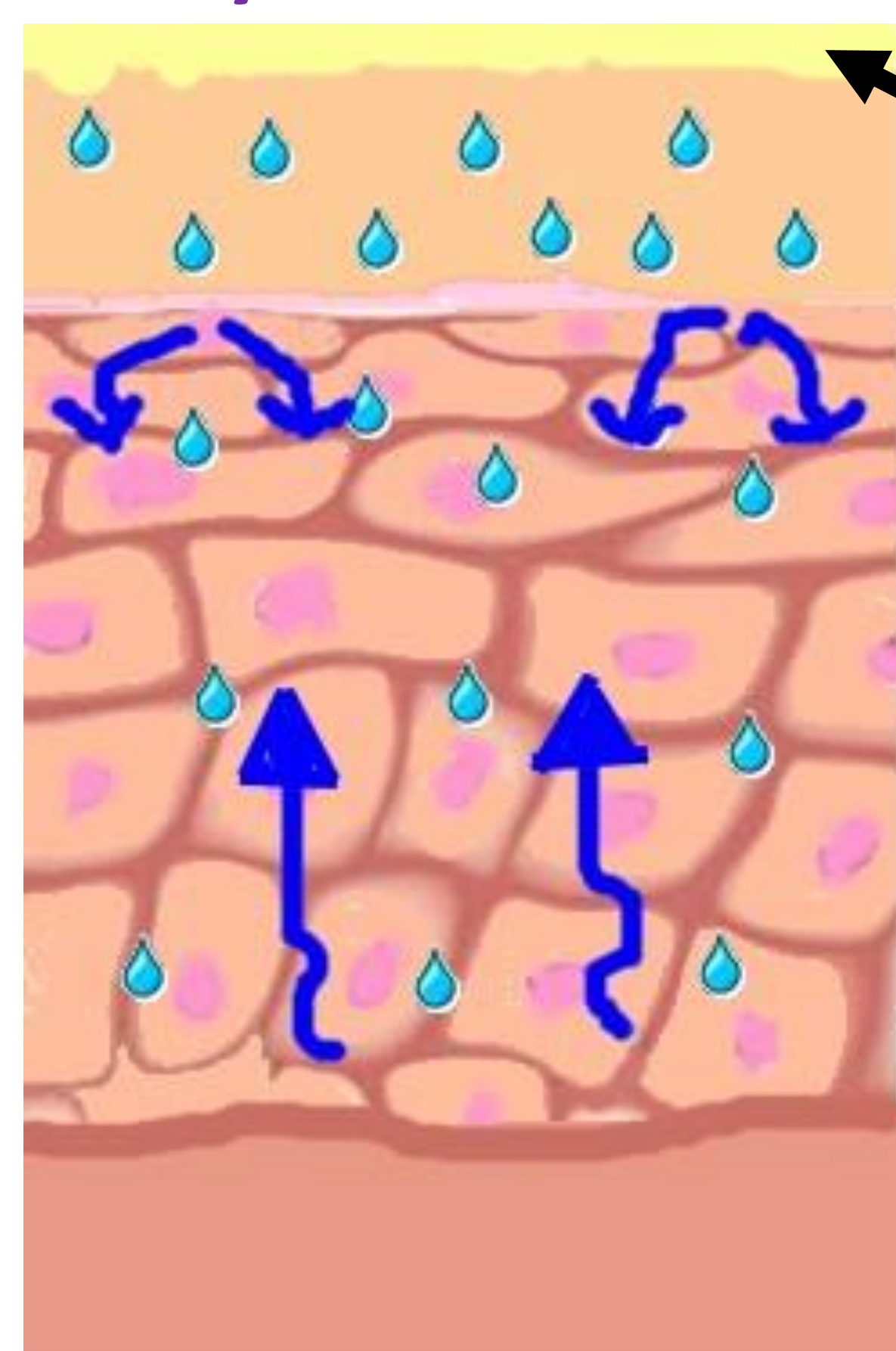
## Purpose

To review the most frequently used permeation enhancers in topical preparations in view of their potential role in promoting systemic adverse effects.

## Material and methods

Bibliographic search in PubMed, Google Scholar and Science Direct using the terms «permeation enhancer», «skin permeation», «systemic absorption of topical drugs».

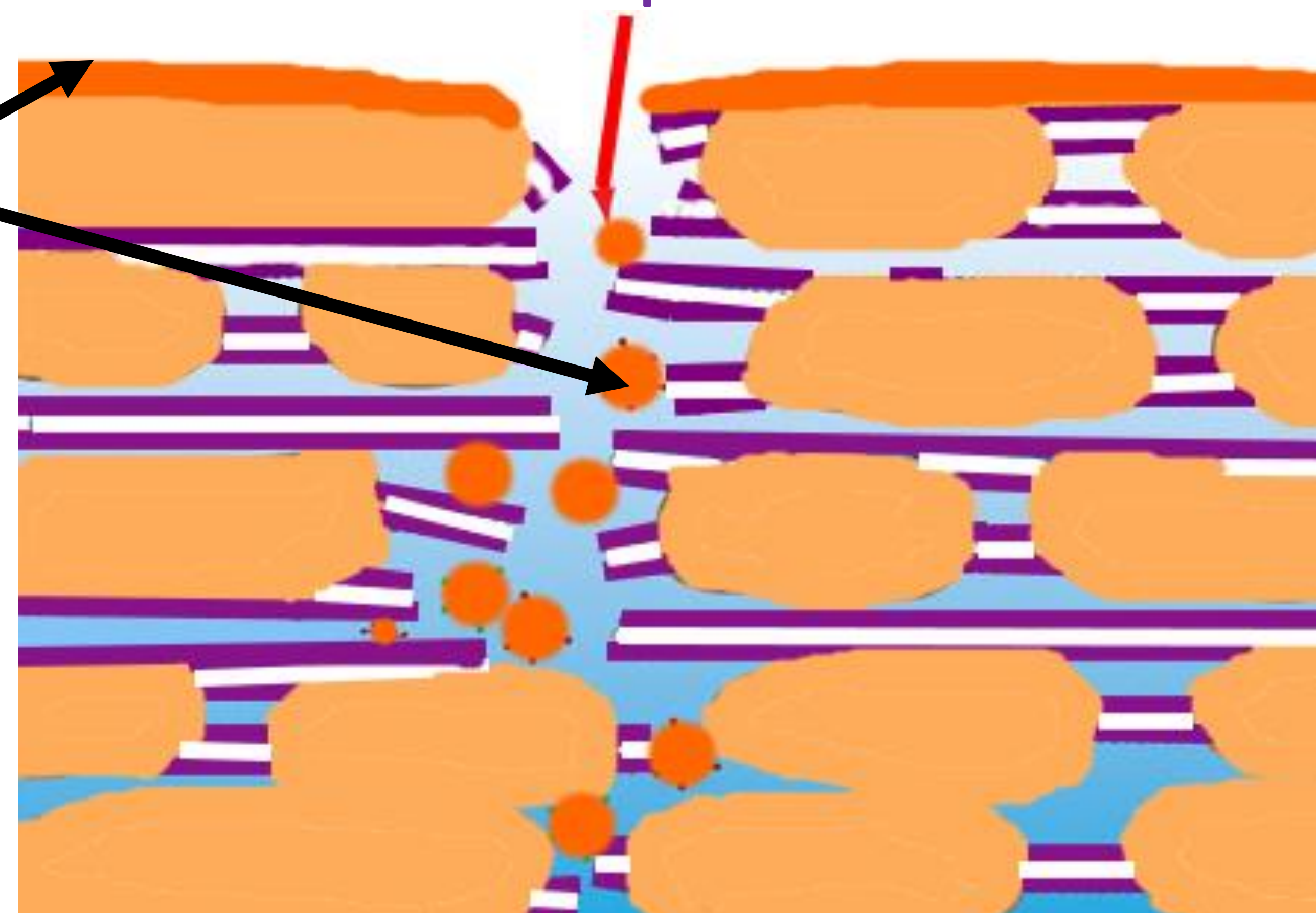
### Skin hydration increase



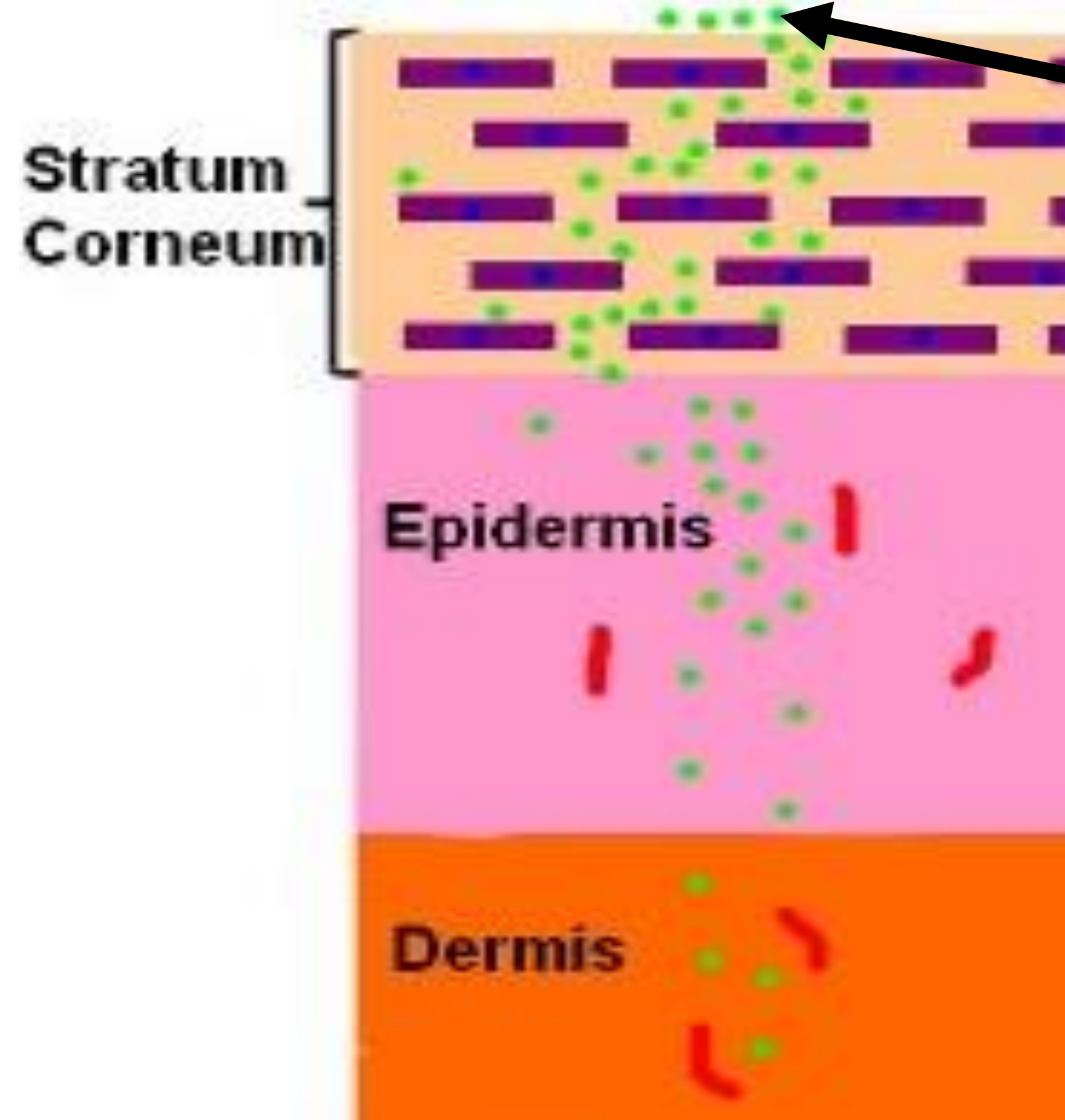
Urea

Amides, used as solvents and that act through drug partitioning improvement

### Reduction of the permeation barrier



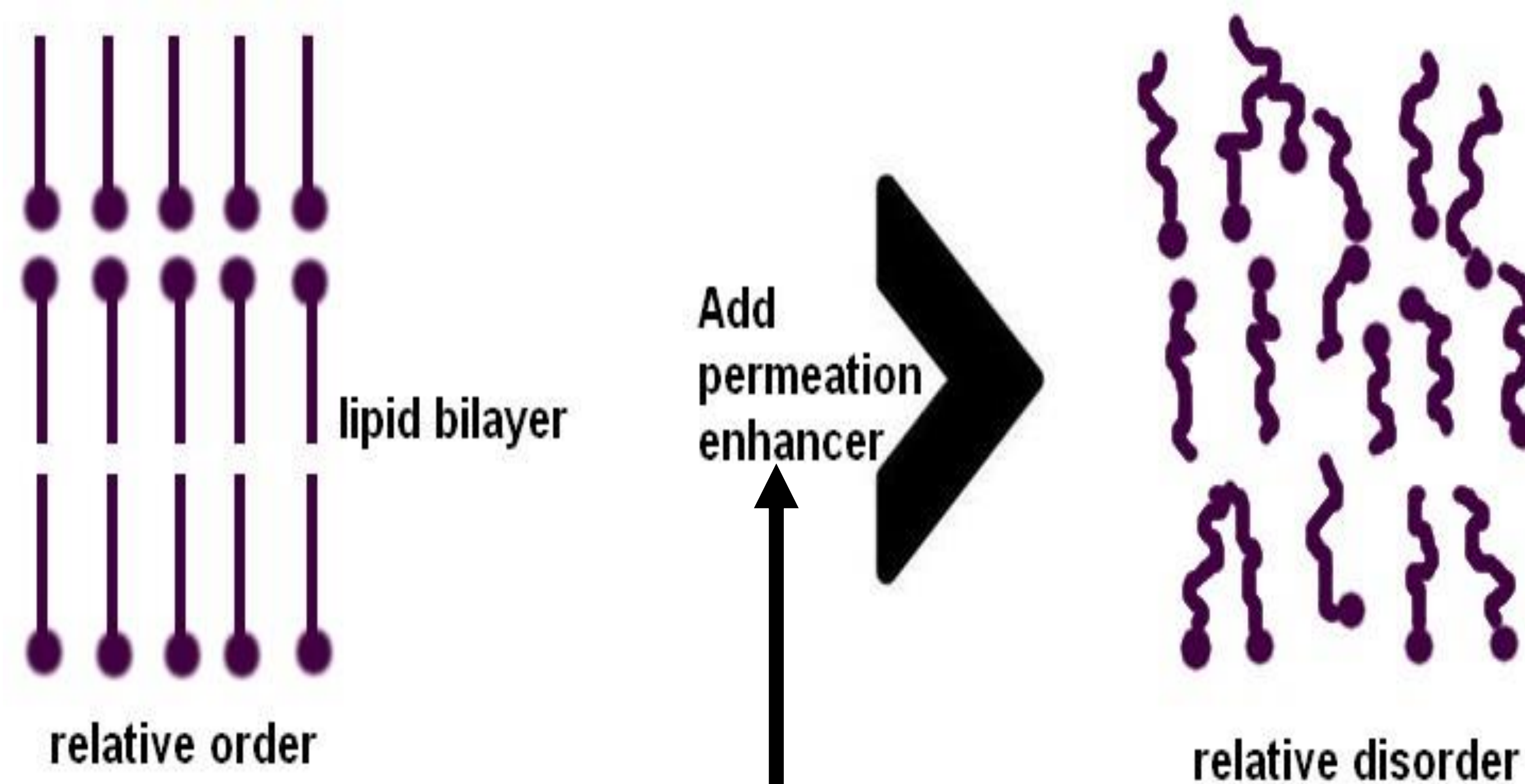
### Substances which pass through the stratum corneum



**Pyrrolidones** (affect hydrophilic and lipophilic drugs);  
**Surfactants** (anionic or cationics, used as emulsifiers);  
**Small peptides** (act by stabilizing structural proteins in the skin).

by interacting with the intracellular keratin

### Modifiers of the stratum corneum



**Essential oils** (Terpenes and Terpenoids);  
**Fatty acid esters** (isopropyl myristate, promote drug solubility);  
**Sulphoxides** (DMSO);  
**Alcohols, Fatty alcohols and Glycols** (ethanol can increase drug solubility and extract some of the lipid fraction from the stratum corneum).

The inclusion of such excipients in topical formulation may therefore influence drug's efficacy and safety. For example, **topical corticosteroids** can cause systemic side effects, especially in children and elderly patients. Vehicles such as propylene glycol and ethanol may increase permeability after prolonged use and very occlusive vehicles might enhance absorption by increasing the hydration of stratum corneum (2).

## Conclusion

The effectiveness and safety of dermatologic therapies depend on both the active drug and the properties of the vehicle. The identification of the permeation enhancers included in topical preparations may be useful for hospital pharmacists in identifying and understanding their potential systemic adverse effects.

## References and/or Acknowledgements

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2 - Dhar S, Seth J, Parikh D. Systemic side-effects of topical corticosteroids. *Indian J Dermatol.* 2014;59(5):460-4.

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