500 Dalton Rule for Intact Human Skin Passive Permeation:

- The molecular weight of a compound can be expressed in Daltons (Da) sum of all the atom weights in the molecule.

- Human skin is an excellent barrier from the environment and topical drugs.
- The *Stratum Conium* (SC) is the main barrier to drug permeation.

- As Molecular Weight increases, skin permeation decreases.

- As molecular weight approaches 500 Daltons, skin permeation approaches zero.

  A small amount may permeate the skin regardless of molecular weight
- Hydrophilic (water loving) topical products will permeate skin less than Lipophilic (oil loving) products.

- Human skin has a superior barrier function compared to any animal skin. Animal skin has little relevance to human skin for transdermal testing.

- Of the 30 or so FDA approved transdermal drugs, all are less than 430 Daltons Molecular Weight.

Peptides are Hydrophilic

Skin care peptides have limited permeation into skin

Dipeptide-2	303 Da
GHK-Cu (Palmitoyl Tripeptide-1)	340 Da
Acetyl tetrapeptide	492 Da
Palmitoyl Tripeptide-5	611 Da
Matrixyl-3000®	
Palmitoyl Oligopeptide	736 Da
Palmitoyl Tetrapeptide-7	694 Da
Acetyl Hexapeptide- 3 (or 8) (Argireline ®)	888 Da
Palmitoyl Pentapeptide-4	802 Da
Acetyl Glutamyl Heptapeptide (SNAP-8)	1,075 Da
EGF -Epidermal Growth Factor	6,045 Da

"There is a large gap for permeability coefficient of major cosmeceutical peptides and proteins and researchers should focus on this ambiguity to find more efficient substances with better permeability." (Gorouhi and Maibach 2009)