



TIOGA RESEARCH
Skin Delivery Innovations


Opportunities for Innovation in Skin-Applied Formulations

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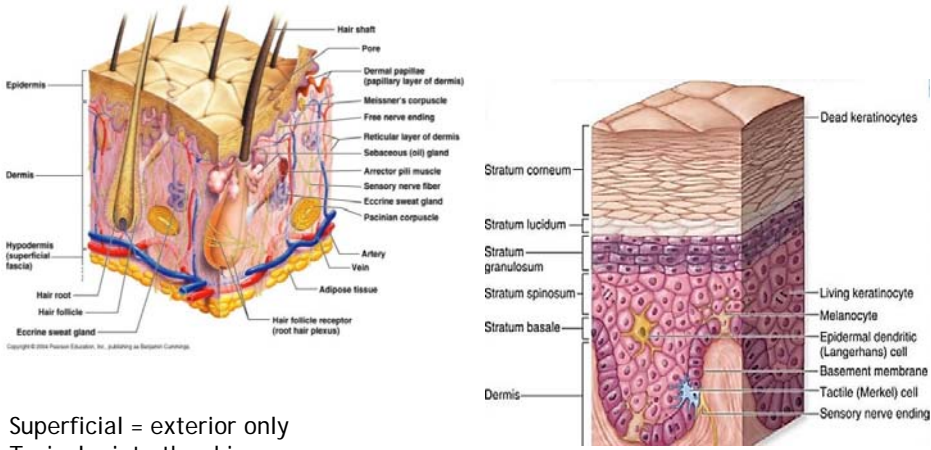
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Topical & Transdermal drug delivery

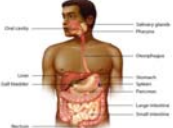


Superficial = exterior only
Topical = into the skin
Regional = through the skin to concentrate locally
Transdermal = through the skin for systemic availability

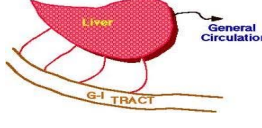
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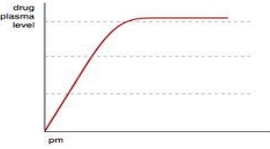
Why Transdermal Delivery?




Avoid gastrointestinal tract




Avoid first pass hepatic metabolism



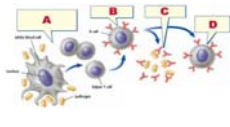
Maintain constant therapeutic level



Avoid need to swallow pills



Avoid unpleasant administration

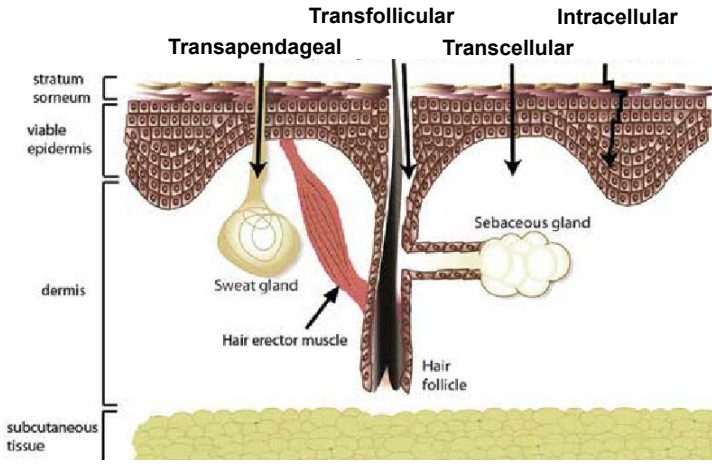


Better immune response in case of vaccines

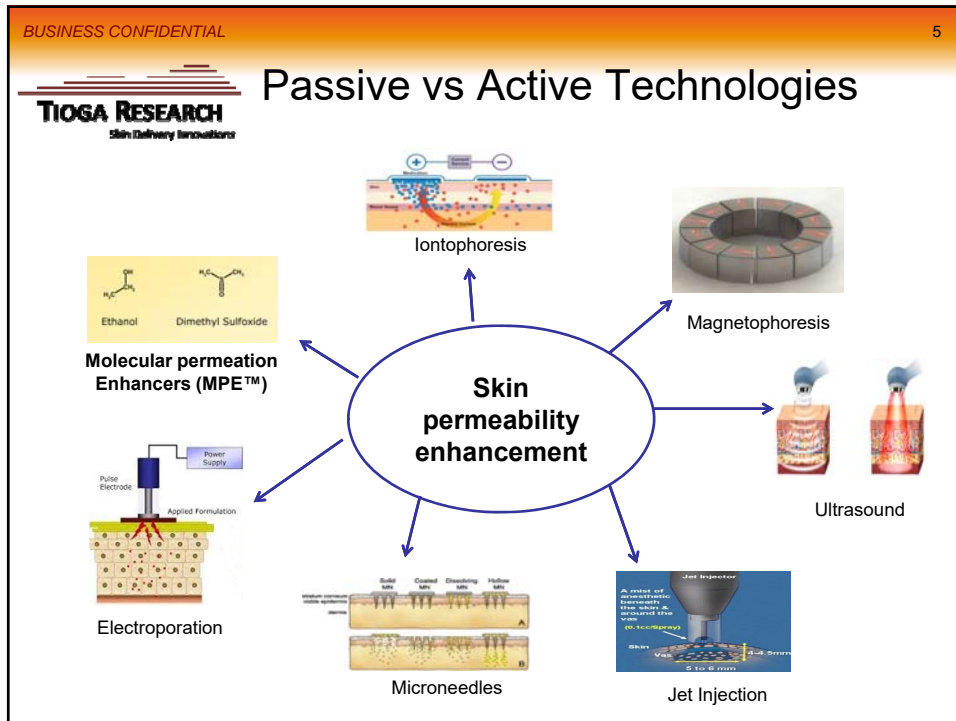
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Drug Permeation Pathways



The diagram illustrates the skin's structure and drug permeation pathways. The skin layers are labeled as stratum corneum, viable epidermis, dermis, and subcutaneous tissue. Three main pathways are shown: Transfollicular (through hair follicles), Transpendageal (through sweat gland ducts), and Intracellular Transcellular (through skin cells). Other structures labeled include sweat gland, hair erector muscle, hair follicle, and sebaceous gland.



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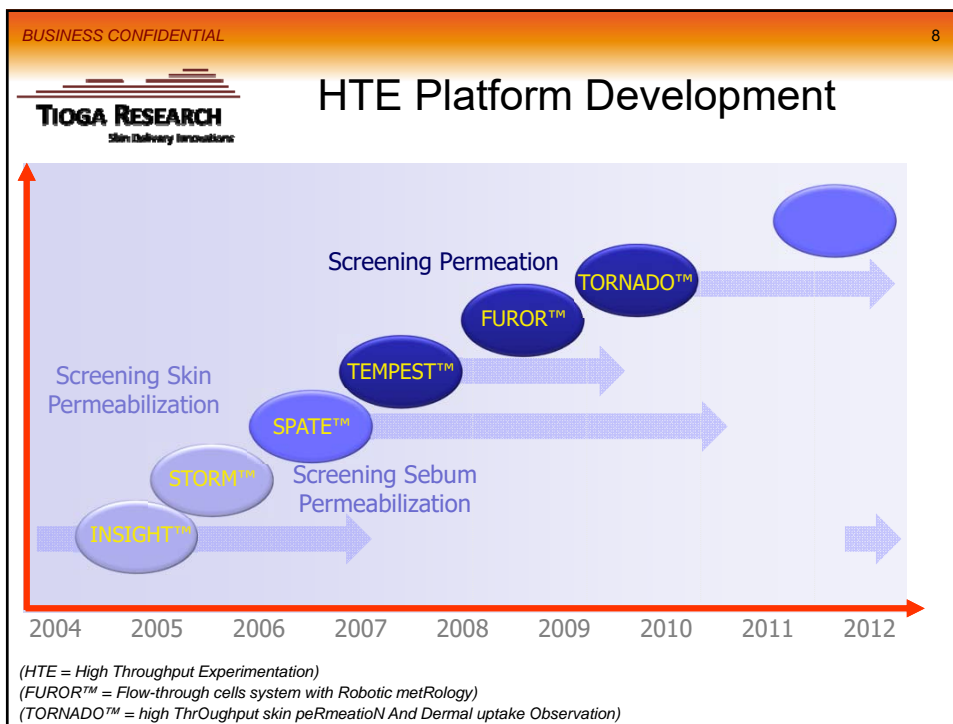
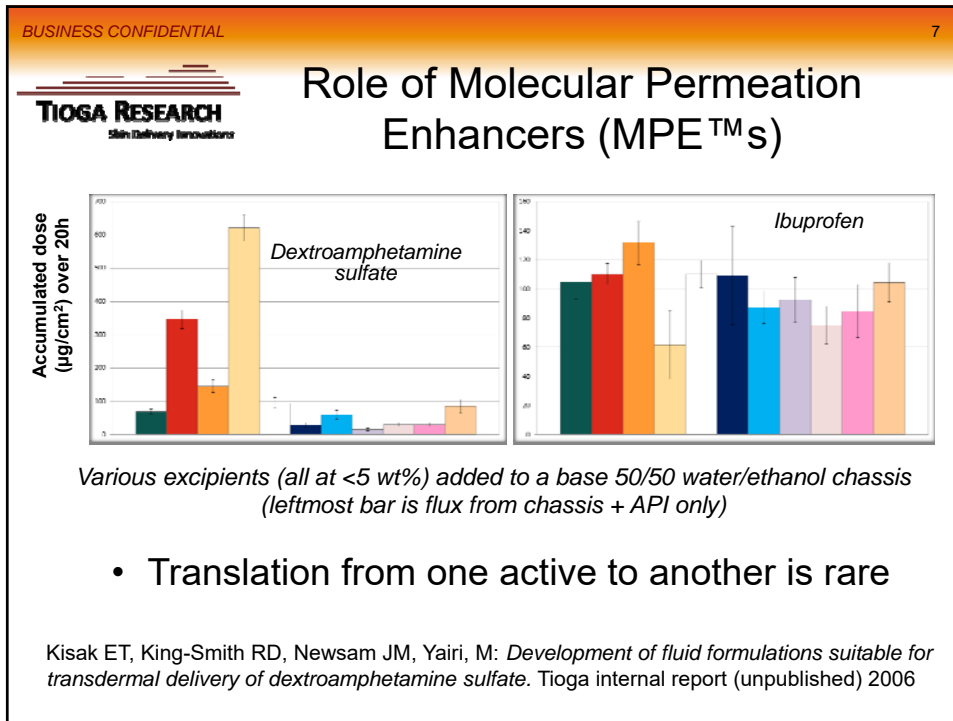
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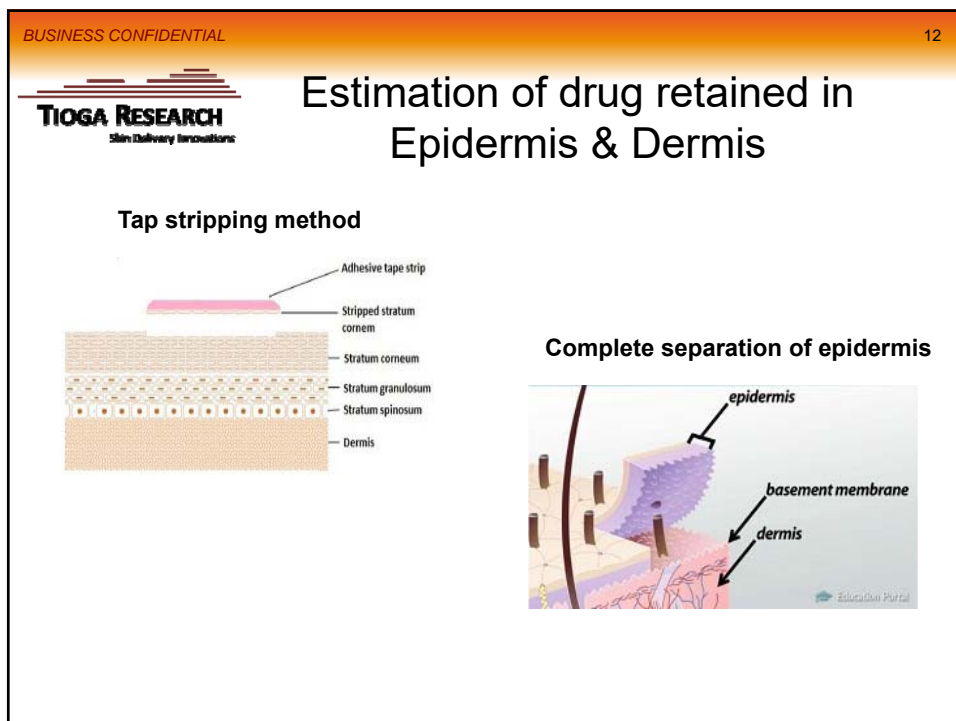
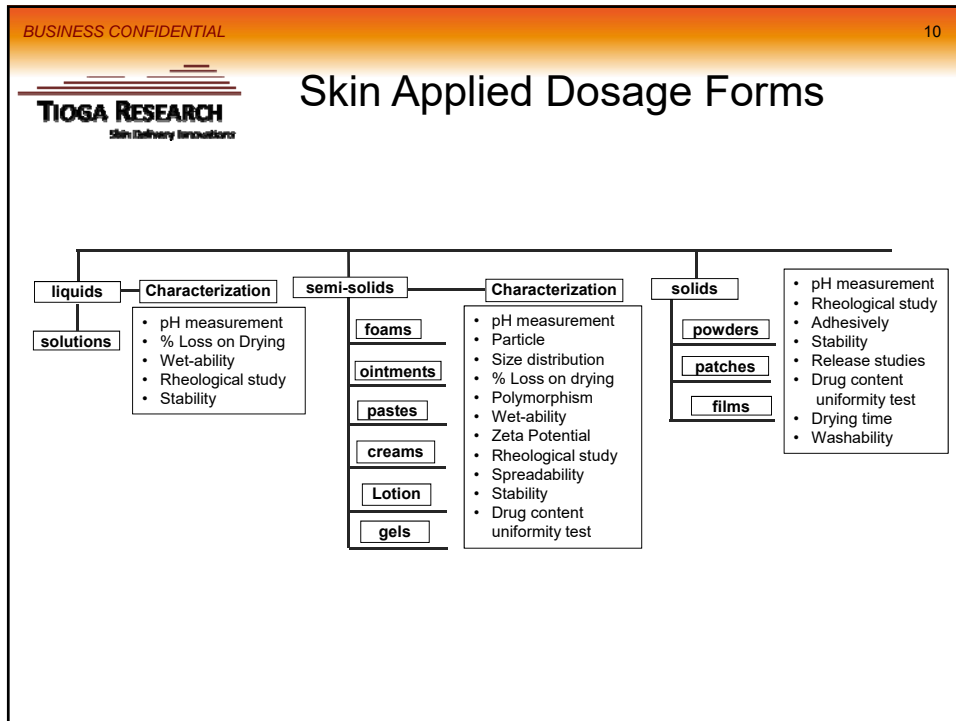
Development of Skin-Applied Product

- **Preferences in drug selection**


Dose	Should be low (<20 mg/day)
Half-life in h	10 or less
Molecular weight	<500
Partition coefficient (Log P)	Between -1.0 and 4
Skin reaction	Non irritating and non-sensitizing
Oral bioavailability	Low
Therapeutic index	Low

- **Development of analytical method (HPLC, LCMS)**
- **Solubility studies**
- **Short term stability studies in solvents**





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Stability studies

Long-term/Accelerated conditions		
	Conditions	Minimum time period
Long-term Testing	25°C ± 2°C/60% RH ± 5%	12 Months
Accelerated Testing	40°C ± 2°C/75% RH ± 5%	6 Months

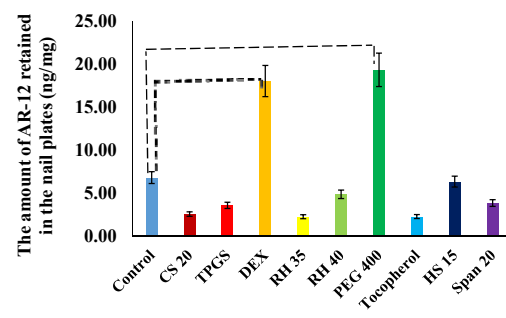
Accelerated conditions		
	Conditions	Minimum time period
Accelerated Testing	low temperature (4-8°C) ambient temperature (25°C) high temperature (40°C or 45°C) freeze-thaw cycles (-10°C to +40°C)	Two cycles every 24 h for 7 days

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Trans-Nail Delivery of AR-12, A Novel Antifungal Drug

Onychomycosis: is an infection in the toe and finger nails that is mainly caused by keratinophilic fungus.



Enhancer	Amount of AR-12 retained (ng/mg)
Control	~6.5
CS 20	~3.0
TPGS	~3.5
DEX	~18.0
RH 35	~2.5
RH 40	~5.0
PEG 400	~19.5
Tocopherol	~2.5
HS 15	~6.5
Span 20	~4.0



Onychomycosis

Results of TranScreen-N for identifying the potential enhancers: CS 20 (Kolliphor® CS 20), TPGS (Vitamin E TPGS), Dex (Dexpanthenol), RH 35 (Kolliphor® EL), RH 40 (Kolliphor™ RH 40), PEG 400 (Polyethylene glycol), HS 15 (Kolliphor™ HS 15). The data represent mean ± SD of three determinations. *p (0.009) < 0.05, ** [p (0.002) < 0.05]


Work performed at Department of Pharmaceuticals, University of Mississippi, prior to joining Tioga Research

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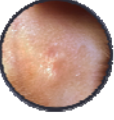




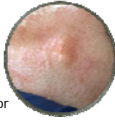


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Treatment of Hypertrophic Scar

- Scar is a **skin fibrotic condition** that can be caused by minor insults to skin, such as acne or ear piercing, or by severe injuries such as burns.
- Scar is mainly formed due to extra deposition of collagen type I and III and reduction in level of collagenase enzyme inhibitor.



Hypertrophic Scar

	1 Day	2 Weeks	8 Weeks
Placebo			
GHL			
			

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Conclusion

- Screening of effective MPE™s
- Selection of an appropriate topical dosage form
- Proper characterization of dosage form
- Stability of drug in formulation
- Translation of *in vitro* data into *in vivo* studies



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