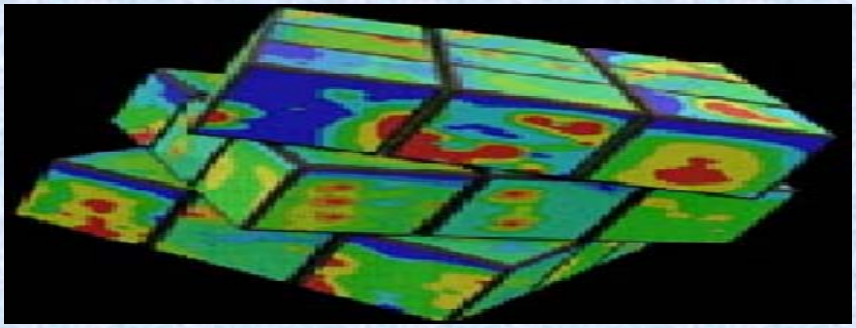
INSIGHT Screening for Synergistic Combinations of Penetration Enhancers



By

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Overview Goals

Transdermal Drug Delivery?

A route that delivers drug across the skin barrier

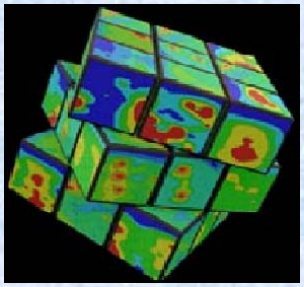
1. Offers painless and sustained administration of therapeutic molecules

2. Avoids hepatic first pass metabolism and gastrointestinal degradation

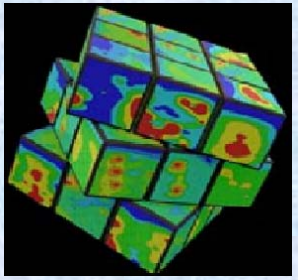
3. Increases patient compliance

Chemical Permeation Enhancers ?

» Chemicals that help to increase the permeability of skin and offer low or no irritation



Objectives



- Finds suitable

  Synergistic **C**ombinations **O**f **P**enetration **E**nhancers (SCOPE) formulations

  Chemical **P**ermeation **E**nhancers (CPEs)

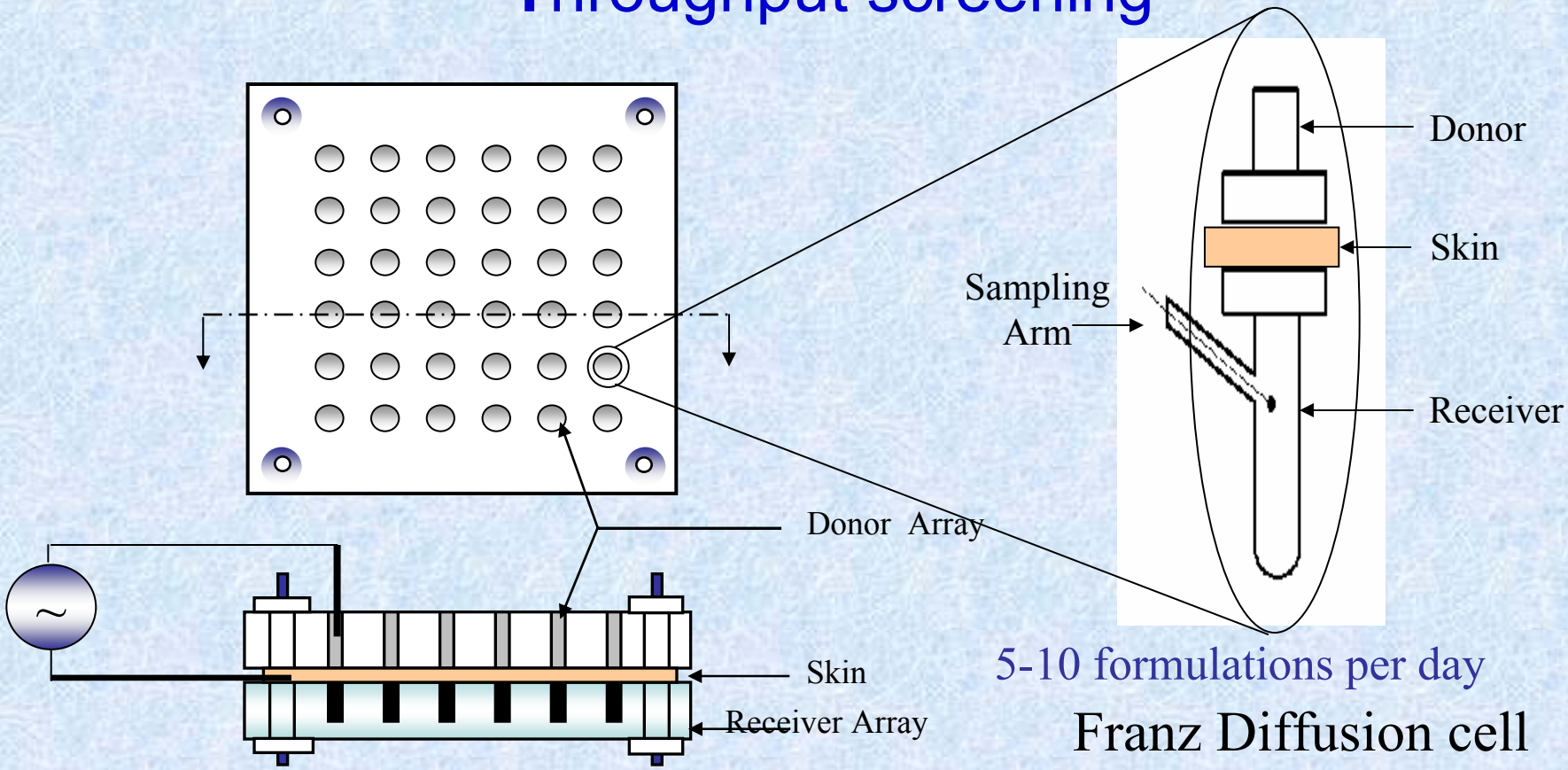
  - Ternary Enhancers

- Uses **IN**-vitro **S**kin **I**mpedance **G**uided **H**igh-**T**hroughput (INSIGHT) screening to determine skin permeability

  - application of HTS tool

- Collect data and analyze Enhancement Ratio

IN vitro **S**kin **I**mpedance **G**uided **H**igh **T**hroughput screening



5-10 formulations per day

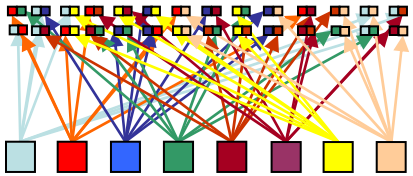
Franz Diffusion cell

1st Gen: 500-1000 formulations per day

*Karande & Mitragotri, Pharmaceutical Research, **19**(5), 2002*
*Karande, Jain & Mitragotri, Nature Biotechnology, **22**(2), 2004*

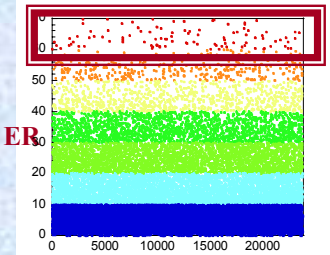
INSIGHT Screening of SCOPE formulations

Successful Formulation

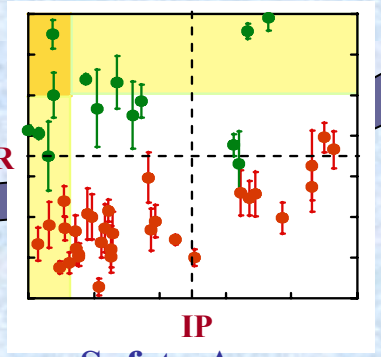


Library Generation

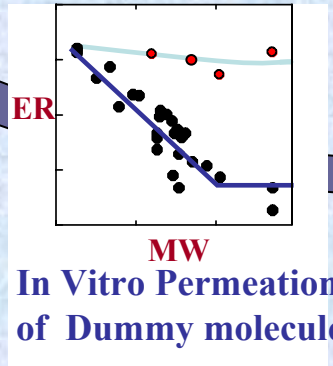
INSIGHT



Epiderm ™



Safety Assay



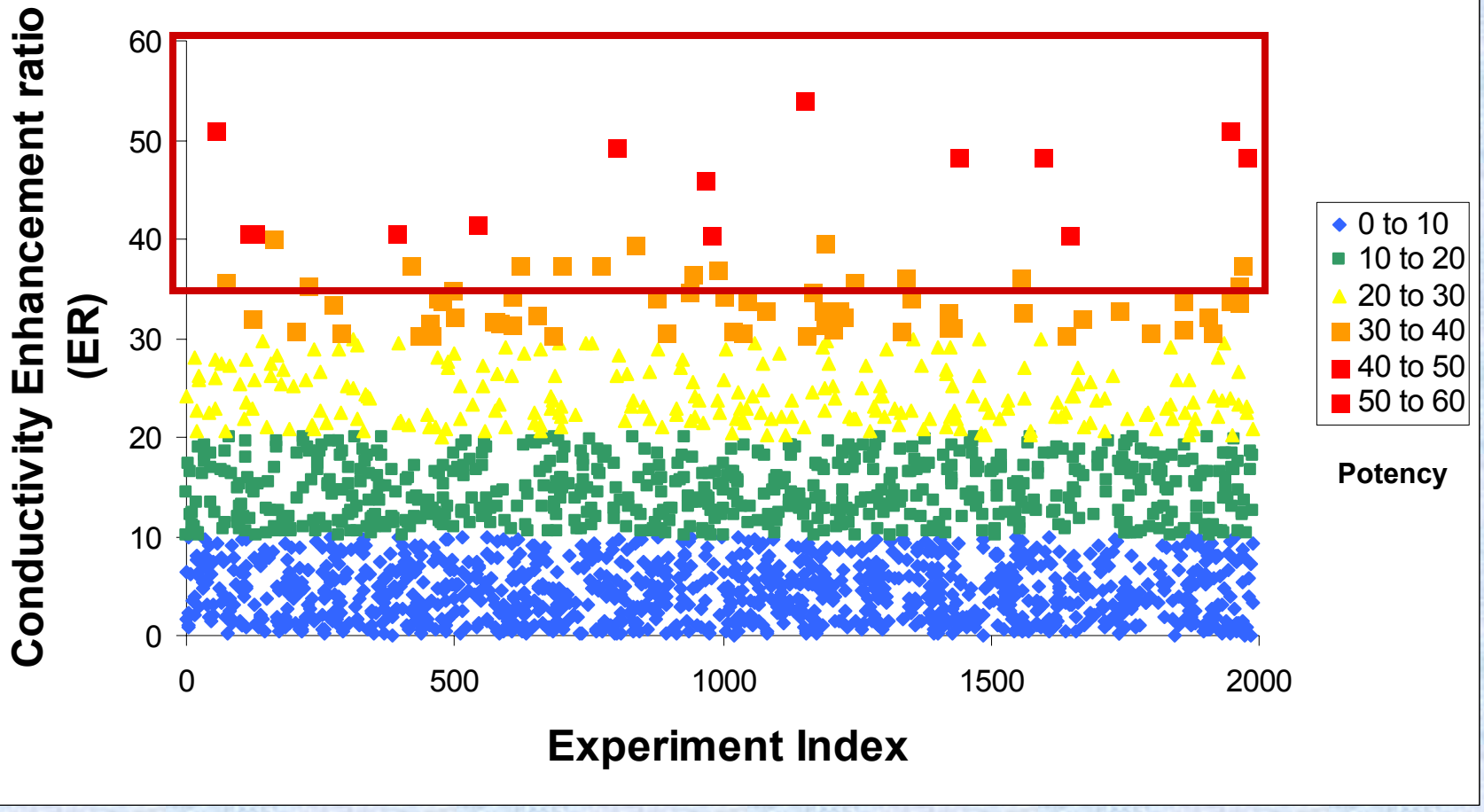
In Vitro Permeation of Dummy molecule

Candidate Drugs

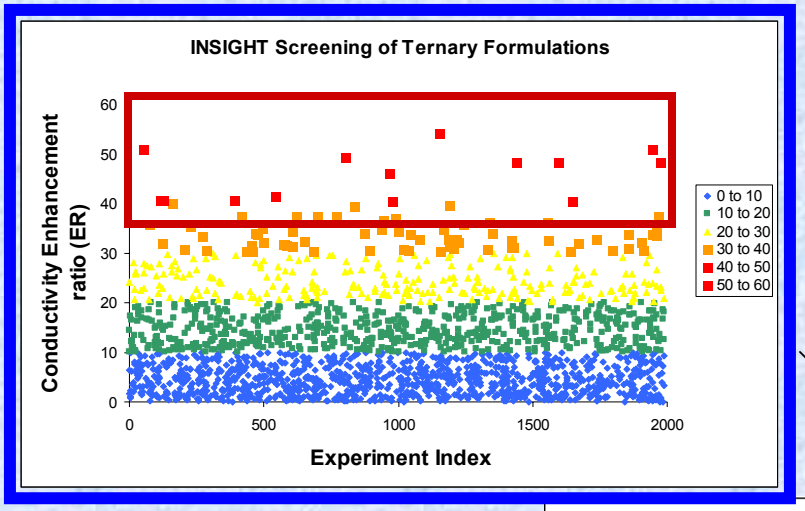
In Vivo Study

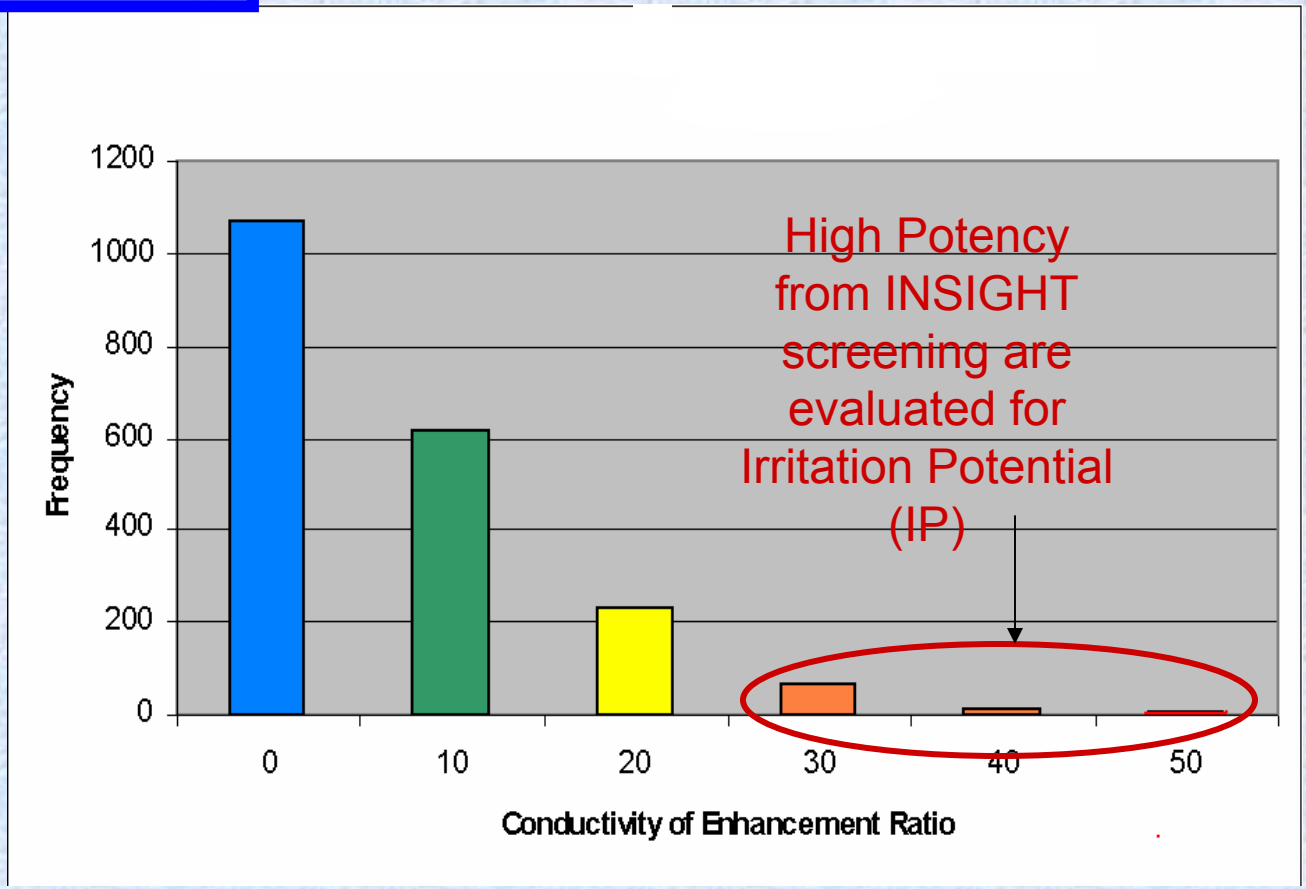
Understanding

INSIGHT Screening of Ternary Formulations

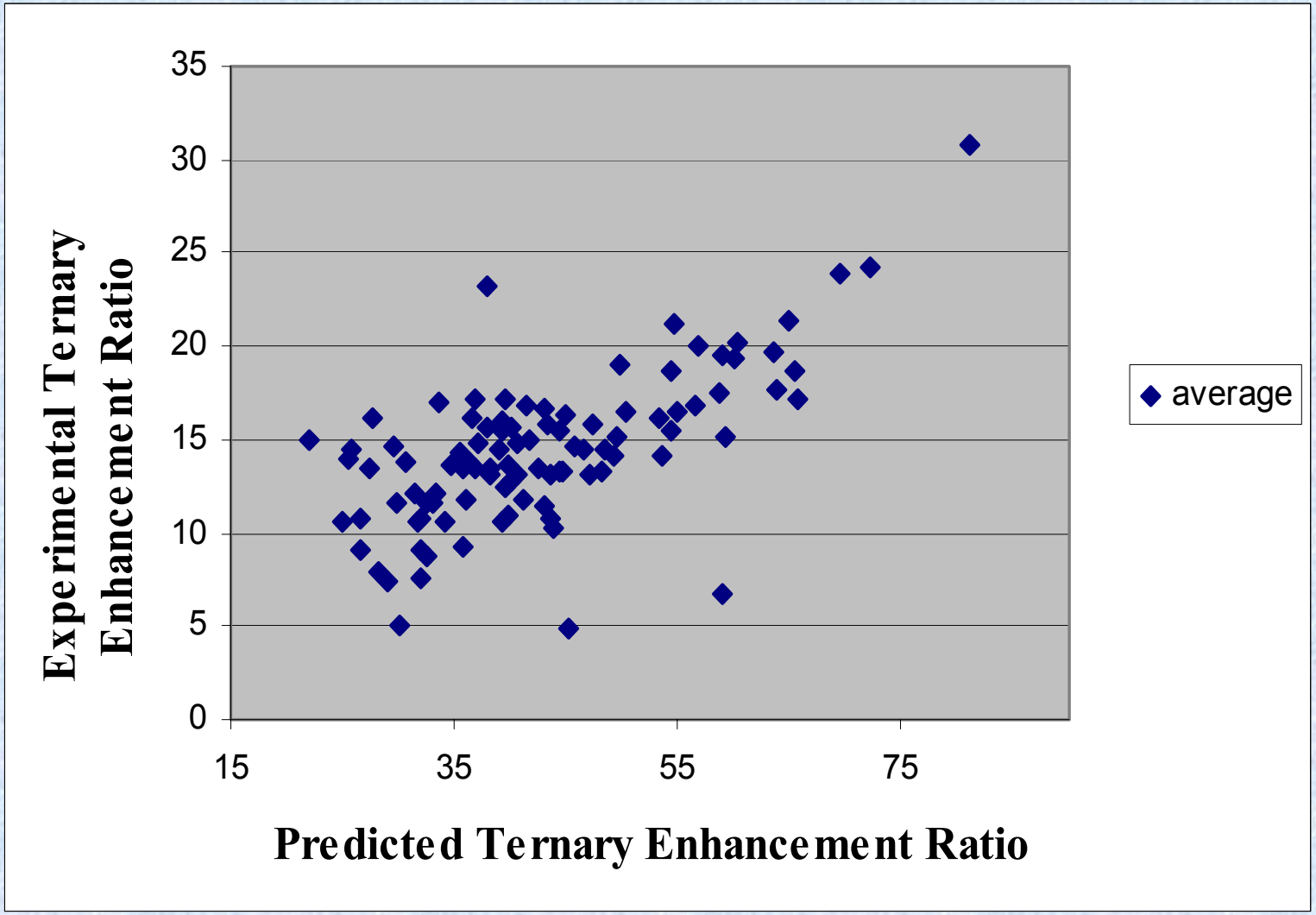


Distribution of Ternary Formulations from INSIGHT Screening





Predicting Ternary Formulation Behavior From Binary Data



Theory Equation:

$$ER_{ABC} = ER_A X_A + ER_B X_B + ER_C X_C + ER_{AB} X_A X_B + ER_{BC} X_B X_C + ER_{AC} X_A X_C$$

ER: Enhancement Ratio

X: Composition

A, B, C: Chemical Enhancers

Achievements

- Found potent ternary enhancer formulations

- Generated Ternary Enhancer data to be used for theoretical predictions

Future Plans

- High Enhancement Potential formulations will be evaluated for Irritation Potential (IP)
- Potent and safe formulations will be evaluated in vitro for flux enhancement using candidate drug
- Successful candidate formulations will be tested in vivo for bioavailability and safety
- Select safe and potent Enhancer Formulations and find why they work so well with FTIR and DLS studies

Acknowledgements

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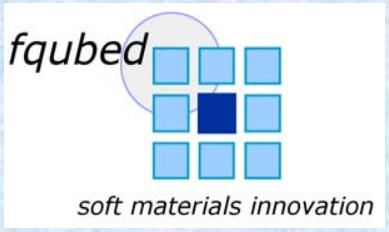
- Center for Disease Control (CDC)
- Fqubed



No More Pain and Pills