



# Meltrex<sup>®</sup> – Drug Delivery as a tool for improved products: The Kaletra<sup>®</sup> Tablet Formulation

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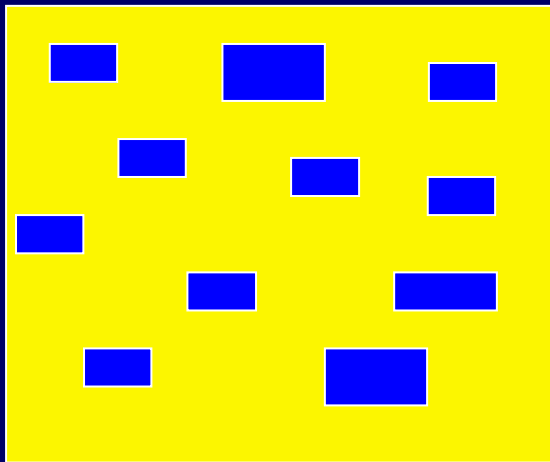


*Solig*  
**SOLIQS**

# Meltrex® Technology: Solid Solution Formulation

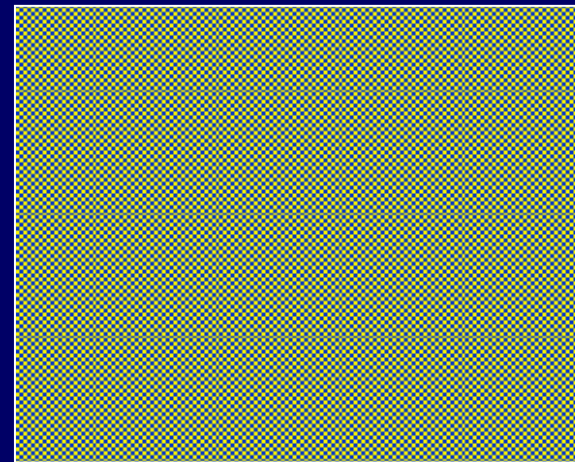
- Melt extrusion technology (Meltrex ®) significantly improves the bioavailability of poorly soluble compounds like LPV/r by dissolving drug in a polymer in a solvent-free environment
  - The drug remains in a state of molecular dispersion as the polymer hardens

Traditional tablet



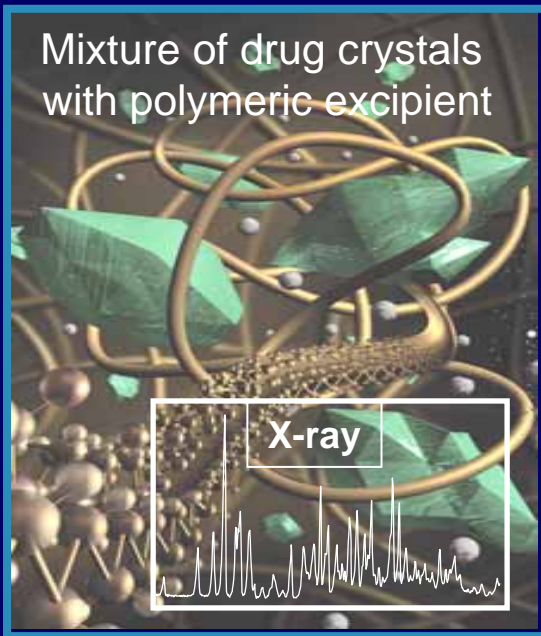
Drug crystals (50 –150  $\mu\text{m}$ )  
mixed with excipients

Solid Solution



Drug dissolved in a hydrophilic  
polymer (glassy solution)

# Meltrex: Formulation Approaches



Tailored release profiles by:

- matrix carrier
- dissolution principle
- disintegration principle



Increased solubility by:

- disrupted crystall lattice
- reduced particle size
- improved wettability
- prevented agglomeration

# Meltrex: Overcoming poor solubility *in vivo*



Meltrex

standard

# Meltrex: Overcoming poor solubility *in vivo*

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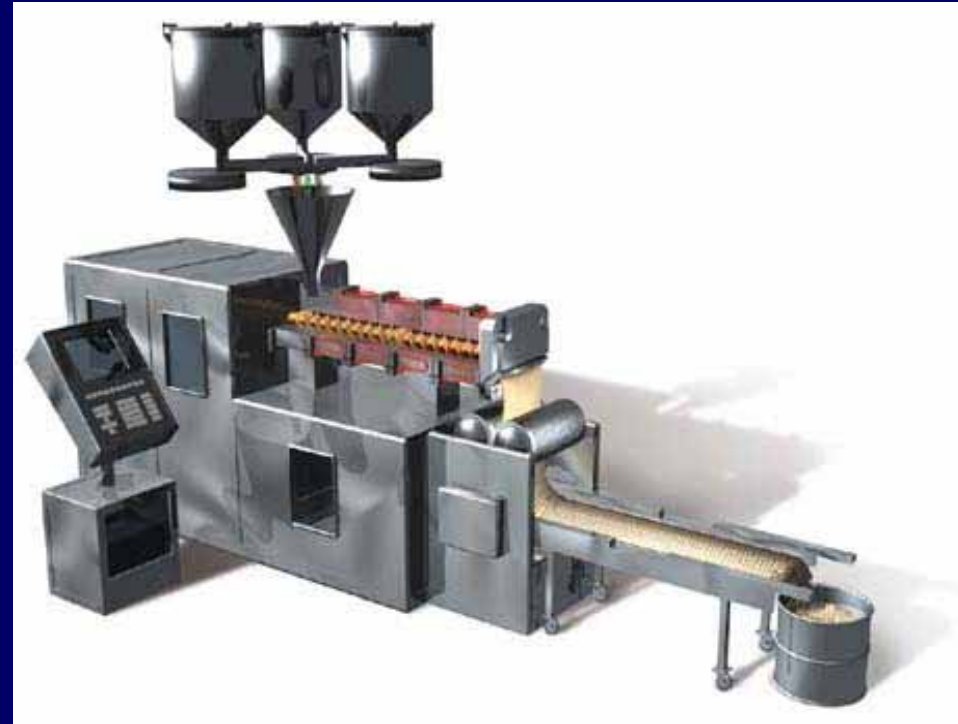
## Meltrex tablets in the GI tract

- Release of nanoparticles from a Meltrex tablet splinter after contact with dilute HCl watched under the microscope
- Continuous release of drug nanoparticles while tablet erodes

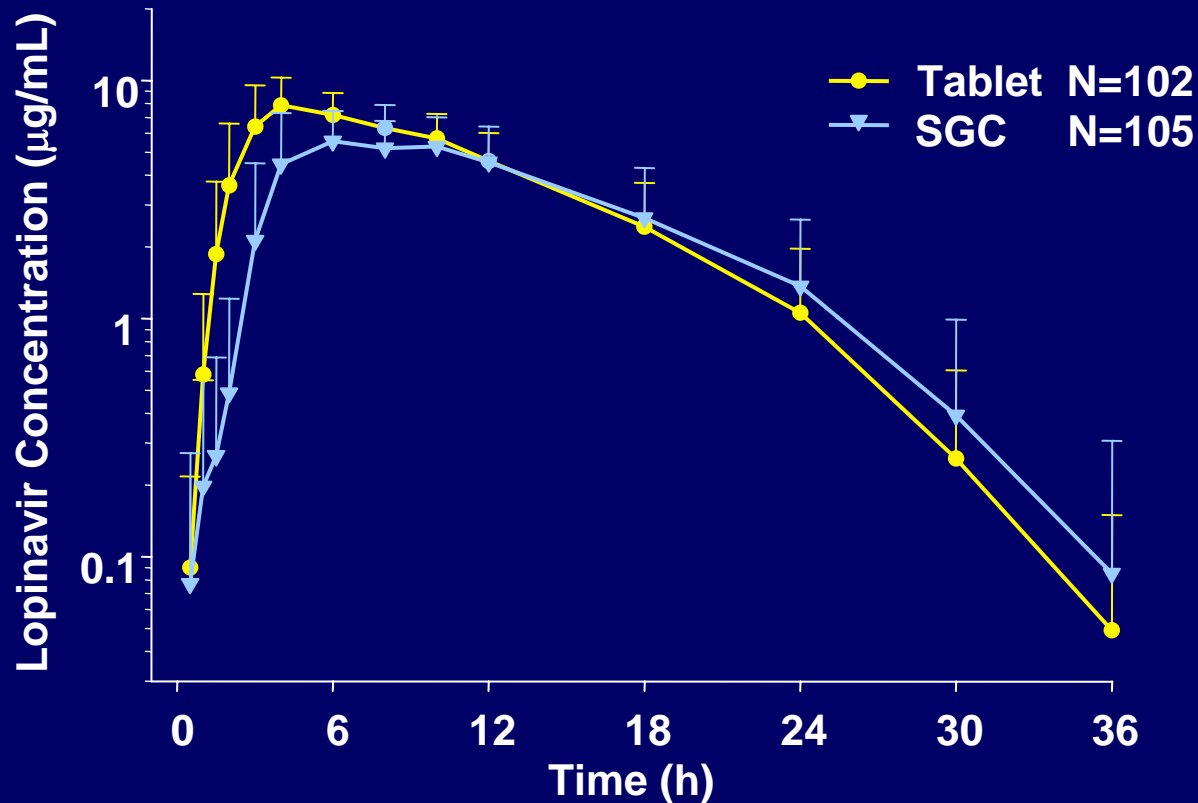


# Meltrex: Manufacturing Process

- Well-established process in chemical engineering, food and plastics industry
- Adapted to the manufacture of pharmaceutical formulations
- Solvent free manufacturing option for Solid dispersion systems



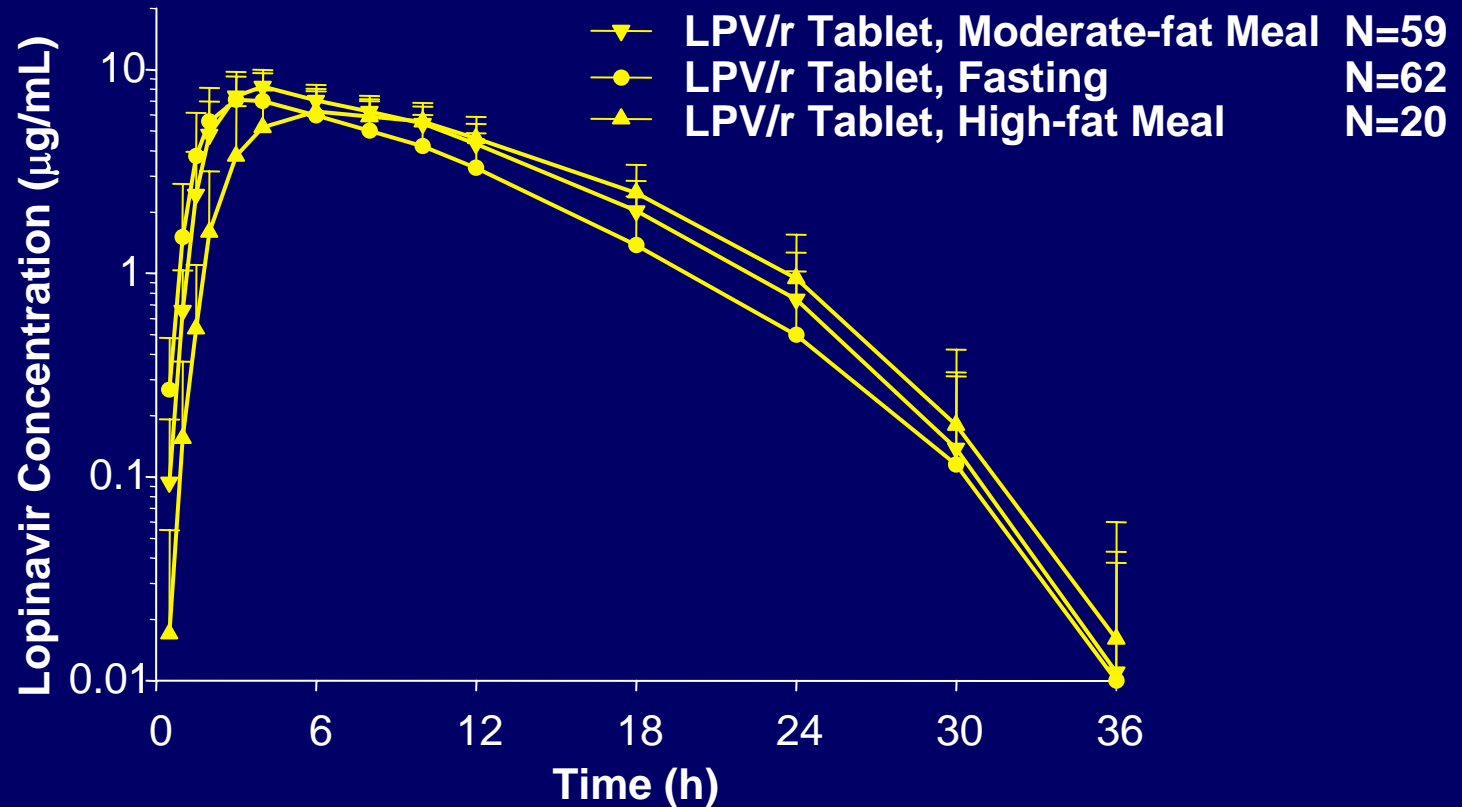
# Lopinavir Concentration Time Profile Following Single Dose LPV/r 400/100 mg Tablet or SGC



Following a single dose of LPV/r 400/100 mg, the tablet provides similar lopinavir exposures to SGC under moderate fat meal conditions (500-600 kcal, 20-30% from fat)

Awni W. *et al.*, 3<sup>rd</sup> IAS, Rio de Janeiro, Brazil, 2005, #WeOa0206

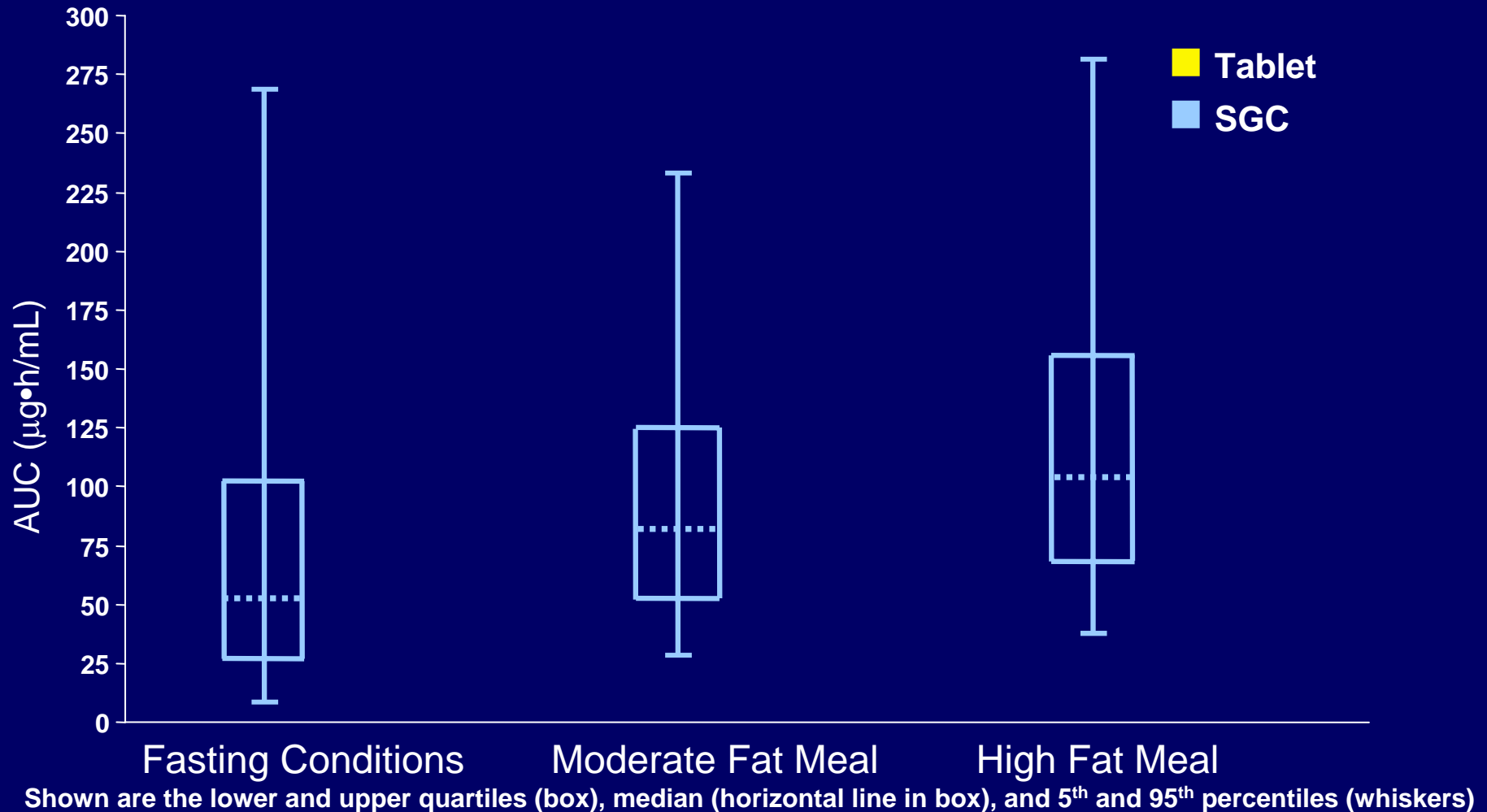
# Effect of Food on Lopinavir Levels – LPV/r Tablet



Following a single dose of LPV/r 400/100 mg, lopinavir exposure from the tablet was similar regardless of food conditions

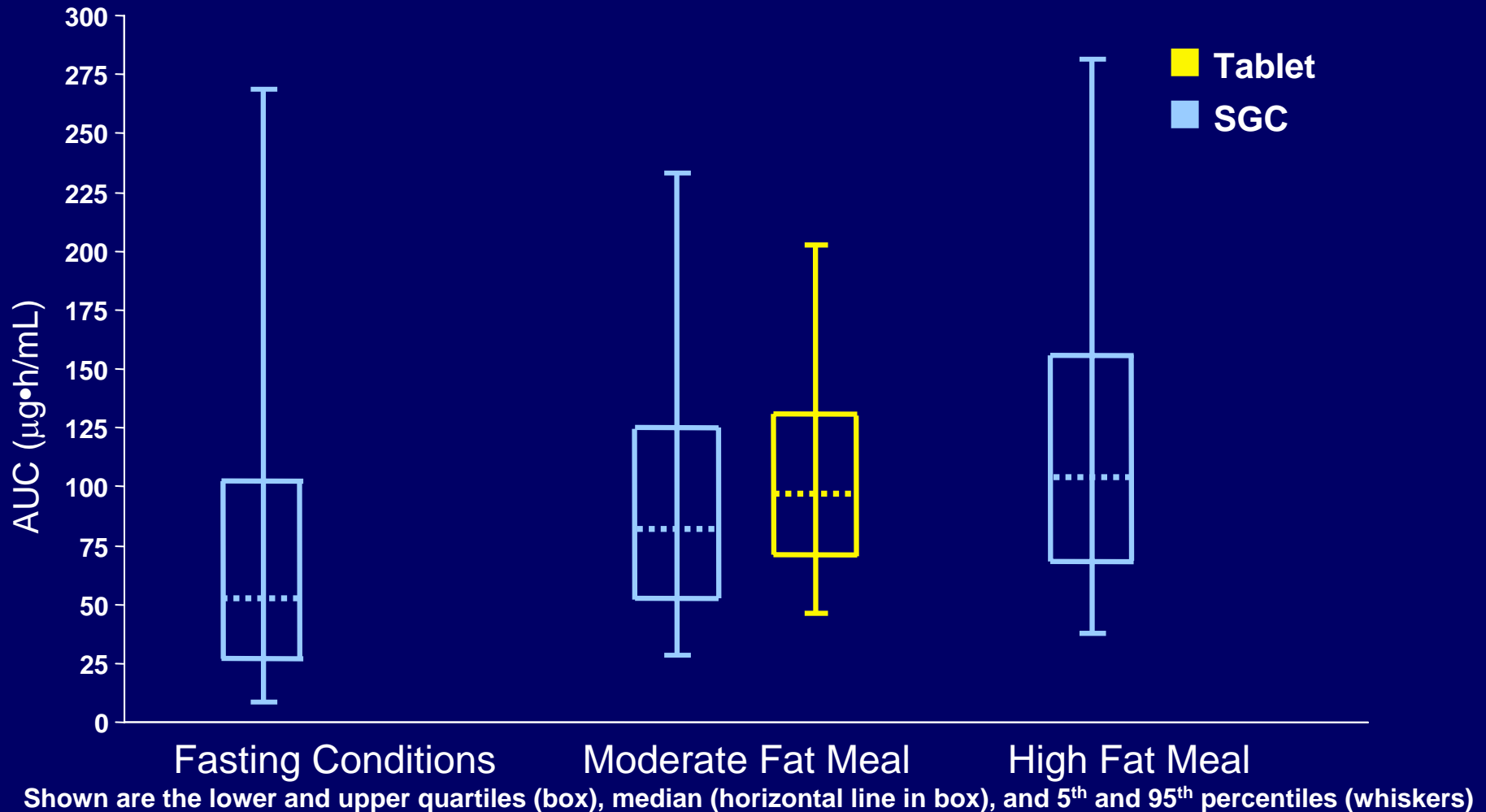
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# LPV AUC from Tablet and SGC Under Various Meal Conditions

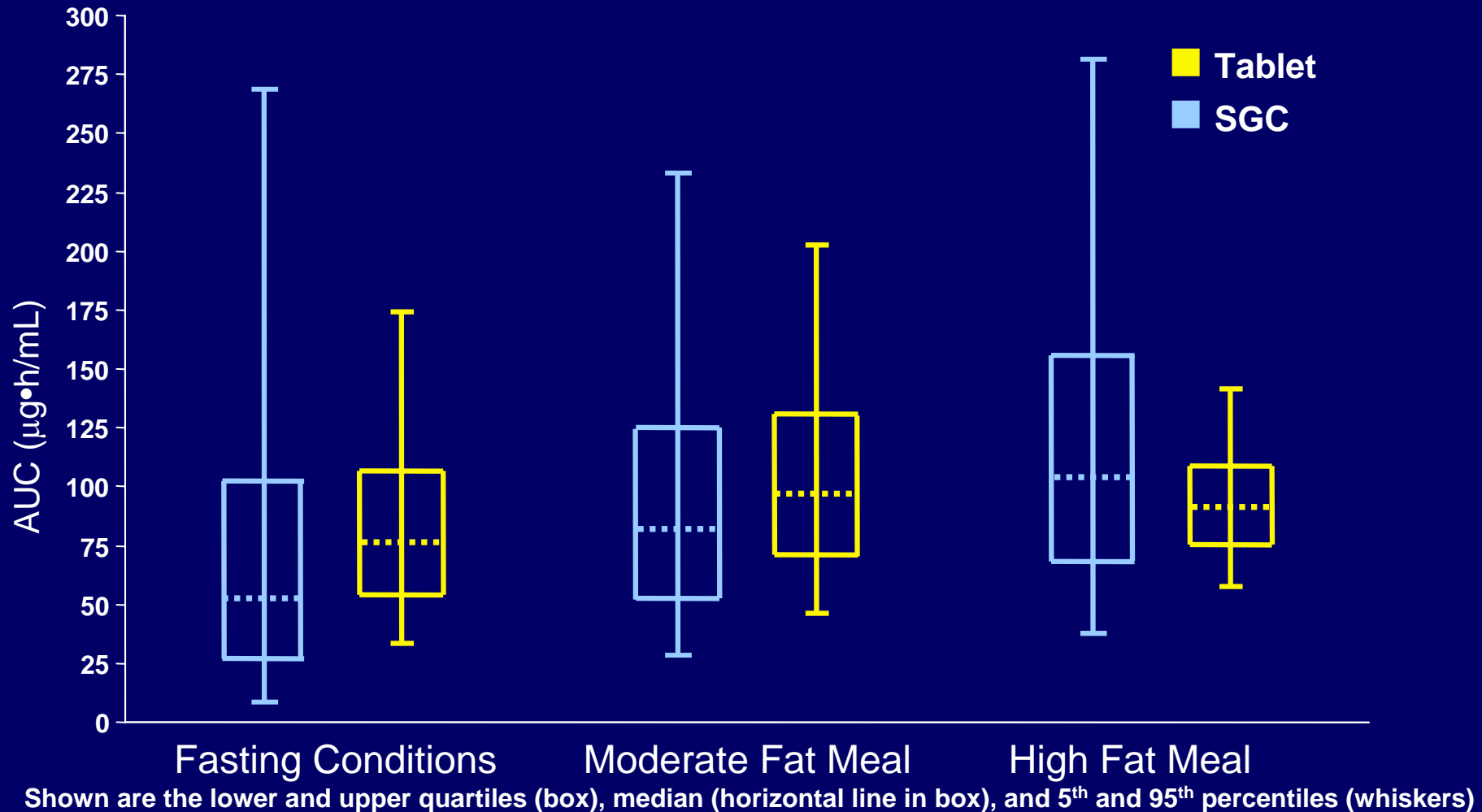


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# LPV AUC from Tablet and SGC Under Various Meal Conditions



# LPV AUC from Tablet and SGC Under Various Meal Conditions



# The Kaletra® tablet

Kaletra is available in 2 formulations

- Soft gelatin capsule (SGC) – 133.3 mg LPV and 33.3 mg RTV per SGC
- Oral solution – 80 mg LPV and 20 mg RTV per mL

Novel tablet contains 200 mg LPV and 50 mg RTV

- Reduced pill count from 6 SGC/day to 4 tablets/day
- No refrigeration
- No refrigeration
- No oleic acid
- Dosing with or without food
- Non-animal sourced excipients

**SGC**



**Tablet**



# Conclusions

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- Benefits of the tablet formulation include reduced pill count, room temperature storage, considerably reduced food effect and lower variability of LPV levels compared to the SGC
- The tablet formulation shows ~18% increase in LPV bioavailability relative to the SGC after a moderate fat meal
- Despite this modest increase in average bioavailability, the tablet is expected to produce narrower ranges of LPV concentrations than the SGC with fewer patients likely to be exposed to very high or very low LPV concentrations
- The tablet is also expected to provide more consistent LPV and RTV levels day-to-day as meal conditions vary



“We provide solid solutions for insoluble substances”™

Vielen Dank für Ihre Aufmerksamkeit!