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TABLET LIPID-BASED DRUG DELIVERY THROUGH ADSORPTION PROCESS: DEVELOPMENT AND USE OF A STEPWISE METHODOLOGY

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PURPOSE

This study aims to **develop a methodology for selecting inert carriers to adsorb lipid-based formulations (LBFs)**, thereby **optimizing the oral bioavailability of BCS Class II/IV APIs in tablet formulations.** Specifically, a modified Selection and Development Matrix for Solid Liquid Adsorption (SeDEM-SLA) was utilized, evaluating the mechanical and flow properties of loaded carriers alongside biorelevant dissolution data.

METHODS

Previous works [1] [2] have studied the solubilization and in-vitro behavior of Ticagrelor solubilized in lipidic systems. Based on this prior work**,** a binary mixture composed of 70% of **Labrasol® ALF (Caprylocaproyl Polyoxyl-8 glycerides) and 30% Labrafac ™ MC60 (Glyceryl Mono and Dicaprylocaprate) was used as lipid vehicle for our investigation**. To limit the size of the final unit dose**, the API was suspended into the formulation** with 23- 29% of solubilized API. The suspension was **further absorbed on the inert carriers.**

Absorption capacity of liquid lipid excipients was determined for Labrasol® ALF and Labrafac ™ MC60 onto **Neusilin® US2 (Magnesium Aluminosilicate), Florite® R (Calcium silicate)and AEROPERL® 300 Pharma (Coloidal silicon dioxide)**. Based on these results, the theoretical absorption capacity for the system Labrasol® ALF 70% /Labrafac ™ MC60 30% was calculated before experimental confirmation. **Ticagrelor release during dissolution testing (500 mL FaSSIF V2)** was quantified via High-Performance Liquid Chromatography (HPLC). Additionally, placebo-loaded carriers were evaluated for flow and compaction characteristics using a modified **SeDEM-SLA methodology** [3]The methodology is ilustrated in Fig 1.

Tabletability profile of placebo-loaded carriers were plotted using Styl'One Nano compression simulator. **Tablets were prepared** by incorporating the carriers through **direct compression** using the same equipment at 70 rpm

RESULTS

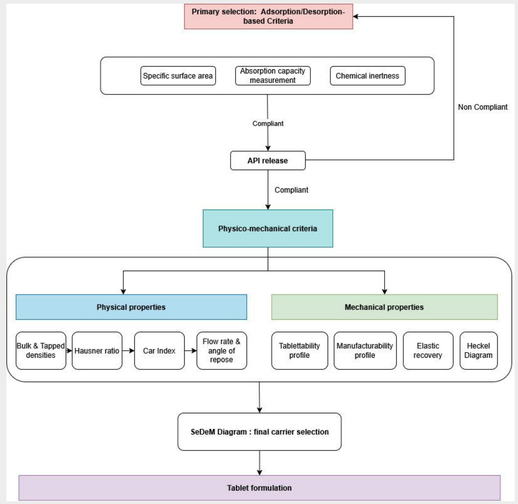


Figure 1 – Schematic representation of the methodology for carrier selection

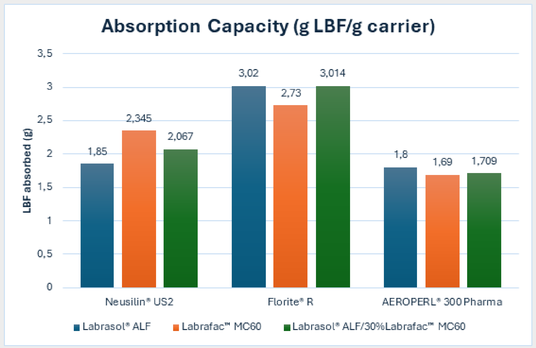


Figure 2 – Lipid based formulation absorption capacity for inert carriers

Florite® R exhibited the highest LBF adsorption capacity, followed by Neusilin® US2. In vitro dissolution in biorelevant FaSSIF V2 media revealed a maximum **Ticagrelor release at infinite time of 80%, 70%, and 60% for Neusilin® US2, AEROPERL® 300 Pharma, and Florite® R, respectively.**

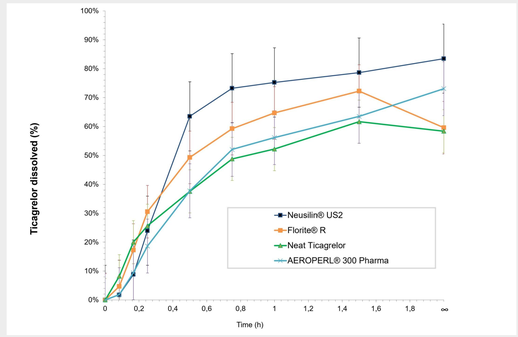


Figure 3 – Dissolution profile for loaded carriers with LBF containing Ticagrelor 500ml, 75 RPM, FaSSIF V2

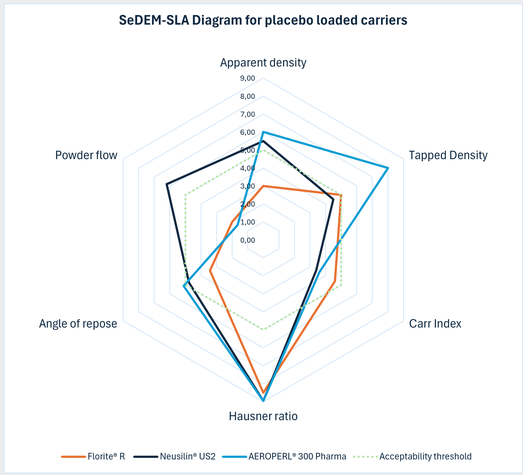


Figure 4 – SeDeM - SLA diagrams for placebo loaded carriers

Regarding powder flow properties, SeDeM-SLA flow parameters (IP, IPP, and IGF) identified Neusilin® US2 and AEROPERL® 300 Pharma as suitable for tableting; however, tabletability profiles showed that the latest was uncompressible, consequently**, Neusilin® US2 was selected for the final formulation**, composed of Microcrystalline cellulose as diluent, polyvinylpolypyrrolidone as binder and glyceryl dibehenate as lubricant. **900 mg Oblong tablets were obtained via direct compression** with a mean hardness of 69,5 N, friability of 0,14% and desintegration time of 21 seconds.

CONCLUSIONS

Achieving efficient drug release from an inert carrier is just as crucial as optimizing its adsorption capacity**. Integrating a lipid matrix** consisting of Labrasol ® ALF and Labrafac™ MC60 successfully **modulated the release kinetics of ticagrelor**, proving to be a highly effective strategy for optimized drug availability.

The application of the methodology described in this study allowed for the selection of suitable carriers for the adsorption of lipidic systems into inert carriers in view of tablets manufacturing. Furthermore, it contributes to **guide the formulation process of tablets using LBF in suspension form as enabling technology for poorly bioavailable** APIs.

This systematic approach guided the development of tablets of acceptable size, through the adsorption of placebo LBFs onto inert solid carriers, successfully establishing **a proof of concept that opens new possibilities for API-loaded solid dosage forms.**

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