

Nano-emulsion Incorporated Oral Thin Film as a novel platform to enhance bioavailability for poorly water-soluble drugs

Yuan Yang, Mickey Lam

8 Tech Innovative, Palm Desert, CA, USA

YYANG@8TECHUSA.COM

Oral dissolvable films have been considered as a unique alternative approach to conventional oral dosage forms. The films could be administered via the gastrointestinal tract as conventional dosages or through sublingual/buccal mucosa membranes which could enhance drug bioavailability by avoiding the first-pass effect and improving permeability due to high blood flow and lymphatic circulation. This work has described a state-of-art technic using nano-emulsion/nano-suspension as a precursor for the film to enhance the bioavailability of BCS class II drugs. The drug molecules are consequentially processed through the emulsification, gelation, and film-casting processes. The gelation process is critical to stabilizing the nano-emulsion for the film-casting as well as controlling the drug release process. Furthermore, the size of the nanoparticle on the film has a strong correlation with the size of the micelles in the precursor and the condition of the gelation process. It has been discovered that nanoparticle from 200 nm to 300 nm has shown the highest permeability for sublingual administration. In one example shown in the work, the bioavailability of a low solubilize drug has been increased from 10% to 34% via sublingual administration of the film. The increasing of the bioavailability was thought to be associated with the enhancement of the diffusion process of the drug in the saliva layer above the mucosa membrane and the fact that the presents of the emulsifier help lose the rigid junction of the mucosa cells.

Introduction

USFDA defines Oral thin films (OTFs) as, “a thin, flexible, non-friable polymeric film strip containing one or more dispersed active pharmaceutical ingredients which is intended to be placed on the tongue for rapid disintegration or dissolution in the saliva prior to swallowing for delivery into the gastrointestinal tract”

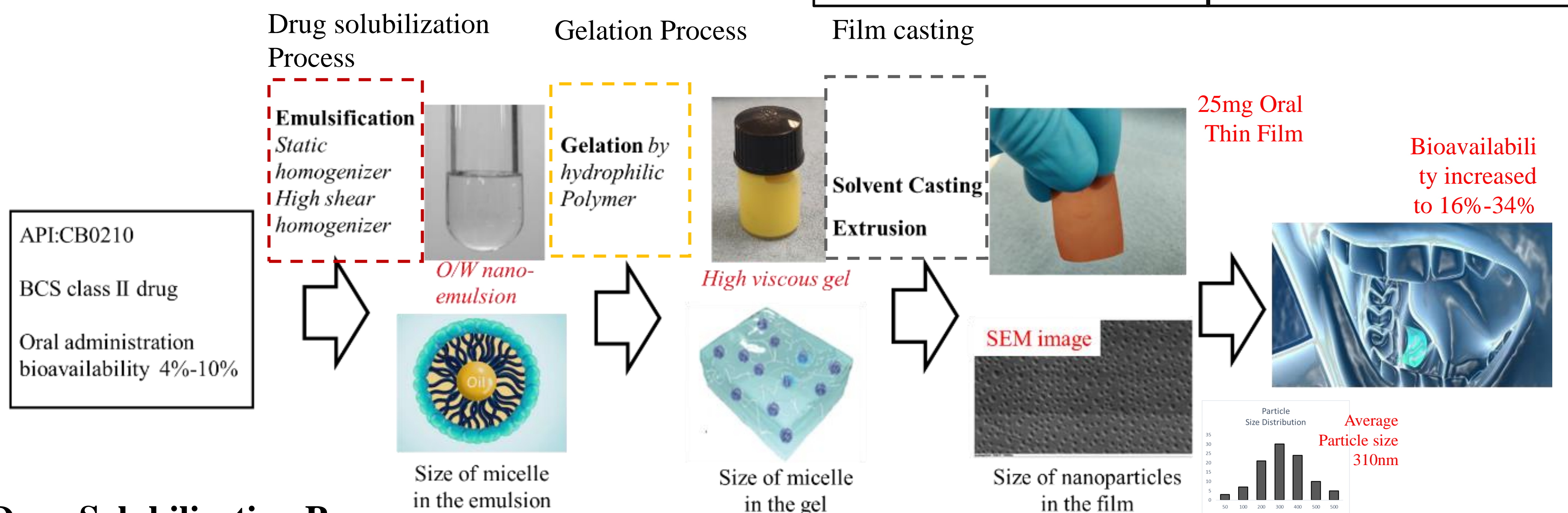
Key Innovation

Three steps Modularized process

- ◆ Drug solubilization
- ◆ Gelation
- ◆ Film casting

Three Pillars for the Platform

- ◆ Nanolization/Micronation
- ◆ Permeability Enhancing
- ◆ Control released film design



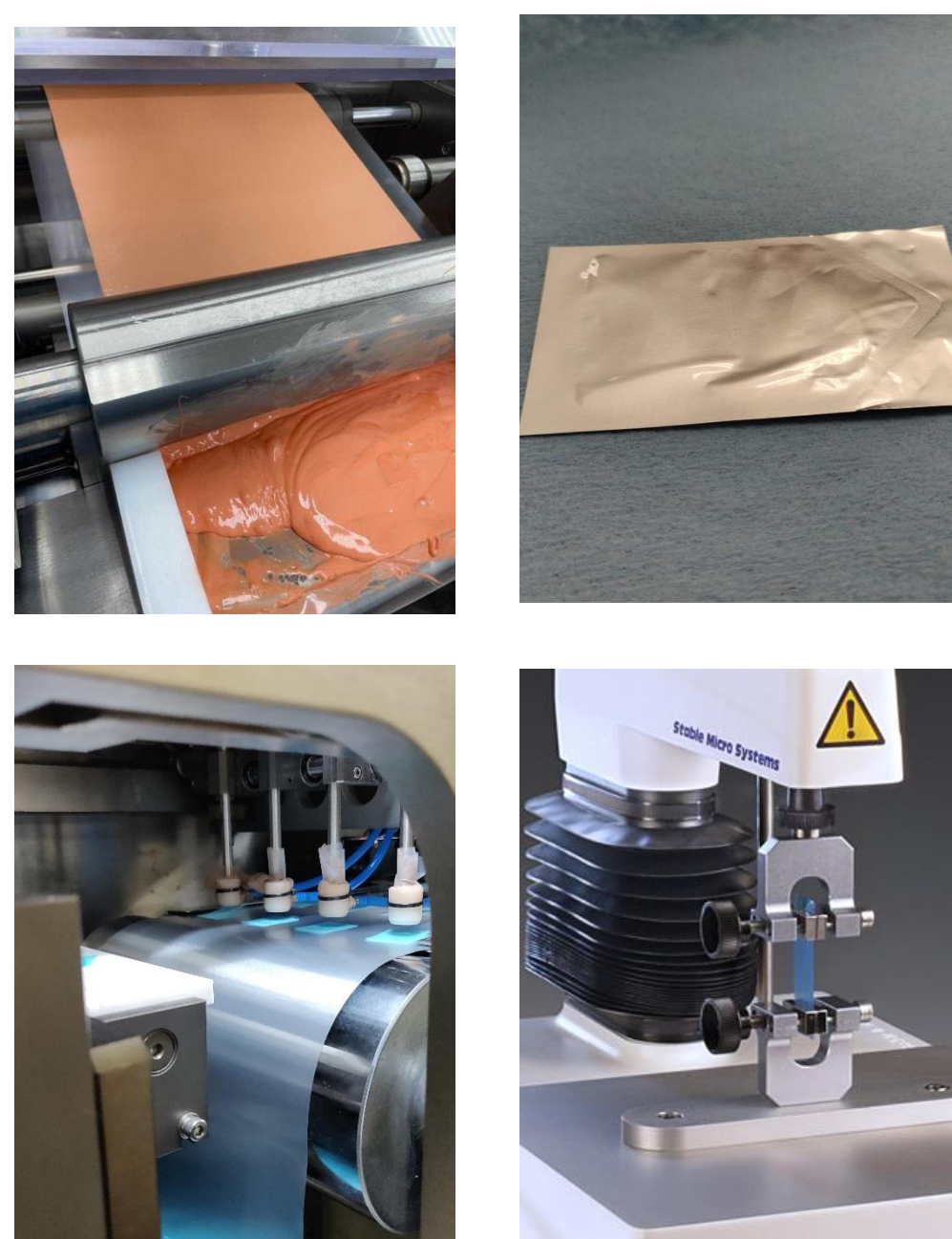
Drug Solubilization Process

For poor water-soluble drugs, micelle and polymeric encapsulation has been proven to be an excellent candidate as precursors for the film. Nano-emulsion and nano-suspension as precursor for the oral film could drastically increase bioavailability of the drug. Nanolization generally being achieved through mechanical methods involving high-shear microfluidizer or high-pressure homogenizer.

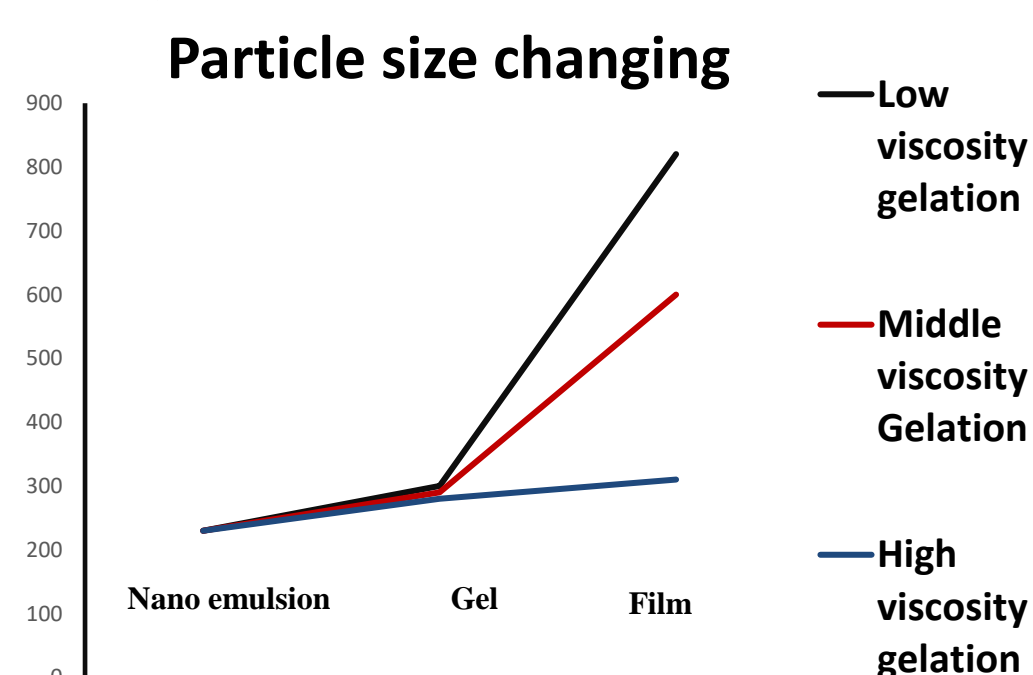
Gelation Process

Gelation with water soluble polymer is crucial to the process. The release mechanism of the film is mainly controlled by the polymer.

Film casting, packaging and characteristic



Film casting could be performed through different methods.
 Solvent casting: Most Versatile
 Hot extrusion: Requirement for heat stability of the API
 Rapid lyophilization: for temperature sensitive and Biological materials



The viscosity of the gel is a key factor affects the particle size in the film casting process.

Characteristic of oral thin film

- Mechanical properties:** Tensile strength, Percent elongation, Young's modules, Contact angle measurement, Folding endurance ...
- Physical properties:** Moisture content, Surface PH, Morphology studies, Palatability study, Thickness and Weight variation ...
- In vitro Test:** Drug content determination, Content uniformity, contamination Tests, Disintegration and dissolution study ...

Tensile strength change as a function of the ratio of plasticizer and film forming polymer