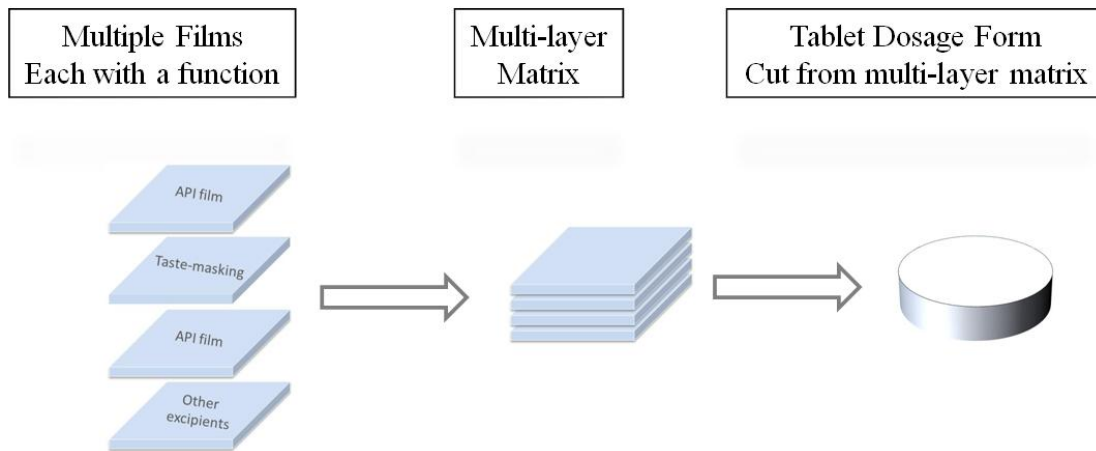


## Prefabricated, film based dosage forms

### Polymer Film, Prefabricated Dosage Forms

Quality by Design (QbD) of dosage forms can be best implemented if the basic formulation of the desired dosage form can actually be designed. We are working on developing oral dosage forms designed as multiple film layers, where each layer has a specific function. The multi-layer dosage forms obtained have similar look, feel and size as a regular tablet, but are made put together in a completely different way. Each layer in the layered dosage form is in place to perform a function: drug carrier layer, solubilizing layer, taste masking layer, etc. The figure below illustrates the concept:



Edible polymer films offer many advantages for delivering drugs. However, film based products such as orally disintegrating films (ODFs) for drug delivery have great potential but also have three major shortcomings:

#### 1) *Thin strip products are designed as orally disintegrating films*

The fact that the film needs to be disintegrated (and the drug dissolved) in the mouth is a severe limitation when the drug needs to be released in the stomach, the intestine or the colon. Furthermore, ODFs are limited to immediate release, not suitable for situations where delayed or sustained release is desirable.

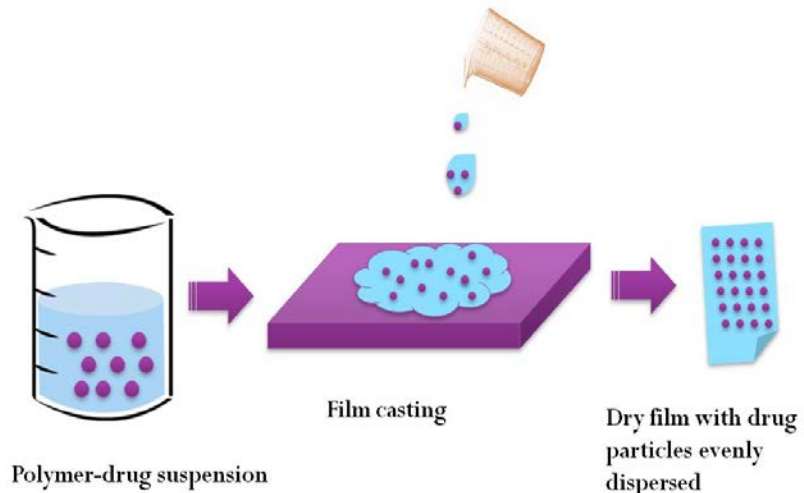
#### 2) *In thin strip products, the active is dissolved in the polymer gel*

Many drugs are poorly soluble, such that they need to be formulated as solids. Fine drug particles, micro- and nano-particles offer a highly technologically advantageous way of formulating poorly soluble drugs. Trapping small API particles in polymer films permits taking advantage of micro- and nano-particles by preventing their natural tendency to agglomerate.

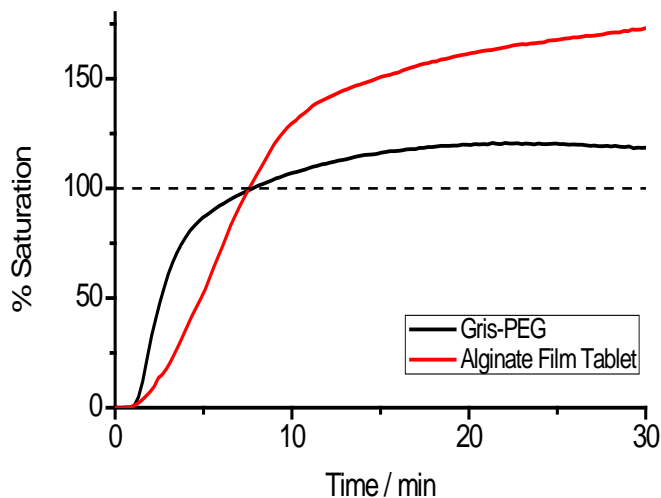
#### 3) *Limited dose of the API*

Polymer films as dosage forms are extremely limited on the dose that can be delivered. For example, Zuplenz, the first prescription based film product is available in 4 and 8 mg doses. Doses of about 20 mg is generally accepted as the high practical dose to deliver in film products

The multi-layer dosage forms address the above shortcomings. The same basic method for making each polymer film is used for the different functions. The method is illustrated in the figure to the right. The same basic manufacturing method is used for the different functions needed in the dosage form. One immediate advantage is that once a film carrying an antioxidant has been formulated, the same film can be used for more than one product. The same can be said about solubilizing agents, pH modifiers, etc.



- 1) The multi-layer dosage form is swallowed like a tablet, so drug release can take place in the stomach, intestine or colon, as required by therapy.
- 2) Polymer films can carry high loads (50% w/w) of particles of API, increasing the possibilities for formulating poorly soluble drugs.
- 3) By using the multi-layer configuration, it is possible to create film based dosage forms for doses of 200 mg or more.



We have produced multi-layer dosage forms containing 250 mg of griseofulvin and compared the drug release rate with the commercially available product GirsPEG<sup>®</sup>. The figure to the left shows the dissolution of the commercial product and of multi-layer tablets. Choosing sodium alginate as the polymer for the drug carrier films results in a dosage form that closely matches the drug release of the commercial tablet. The drug release rate can be modified by changing the chemistry and molecular weight of the polymer used for the film.