smartFilms®—An Alternative Oral and Peroral Dosage Form for an Improved Delivery of Active Ingredients in the Amorphous State

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Purpose
Listerine PocketPaks® Breath Strips were the first commercially available oral film products. Even before and after this launch in 2001, numerous different oral film systems were developed and also patented. However, only a few further products (e.g. Suboxone® Sublingual Film) were introduced. Some products were already withdrawn from the market (e.g. Children's Triaminic Thin Strips®).
Currently, oral films are more a niche product, which only complement the existing product range, not least caused by the following limitations. Oral films are commonly manufactured by solvent casting or hot melt extrusion. Either way, the ingredients are passed through the entire manufacturing process, which leads to stress exposure (e.g. thermal, mechanical). In addition, both methods have relatively smaller output and higher costs than other manufacturing methods of solid dosage forms (e.g. tablets). More importantly, the absolute and relative loading of oral film products are limited, typically rather below 65 mg respectively 30 % (w/w). The smartFilms® technology was developed successfully to overcome these limitations.

Methods
Cellulose based papers were used as fibrous carriers to load various ingredients into their porous matrix structure. The loading step was separated from the subsequent film forming step. Commercially available paper products like tissue papers or filter paper were characterized (e.g. pore characteristics, strength parameters) and then used as preformed carriers. Afterwards the ingredients (e.g. folic acid, diphenhydramine hydrochloride) were applied directly in liquid form onto the cellulose based carrier. The liquid loading (e.g. solution, suspension) was performed with a piston-stroke pipette either at once or in multiple steps until the desired dose was achieved. Afterwards, the solvent or dispersion medium was evaporated at room temperature or in a compartment drier at 50 °C. After drying, the ingredients were embedded in the pore matrix. As final step, the loaded carrier was cut with a scalpel into desired sizes and shapes (e.g. thin cuboid with a surface of 2 - 3 cm²). Structure characterization was performed by scanning electron microscopy, investigation of the crystalline state by x-ray diffraction confirmed by differential scanning calorimetry, adjusting the loading by weighing confirmed by UV-Vis spectroscopy after extraction and determination of in-vitro release by a dissolution paddle method.

Results
The patented smartFilms® technology is a simple and fast process. Only a cellulose based carrier, the desired ingredients, a convenient loading liquid and no other ingredients (e.g. plasticizers) are required compulsorily. However, different ingredients are optionally applicable (e.g. colorants, flavors). They are biodegradable and recyclable dosage forms from renewable sources. Moreover, the smartFilms® can also be placed into capsules or simply after shredding compressed to tablets. Surprisingly it was found, after multiple loadings with aqueous solutions and after drying, the active ingredient remained embedded in amorphous state in the μm-sized pore matrix. By now, avoiding crystallization was only described for materials with nm-sized pores (e.g. smartPearls® technology) caused by space restriction. This amorphous state was found to be stable over twelve months of storage under room conditions. Thus, the smartFilms® technology provides an increased saturation concentration and hence a higher bioavailability of the active ingredient. High absolute loadings over 300 mg/cm² related to the top surface and relative loadings over 80 % related to the total mass were achieved. The loading either high or low can be easily and exactly adjusted to the individual users need. Faster in-vitro release was achieved compared to tablets, because of the amorphous state and the absence of any disintegration time. The active ingredients were released by elution out of the pore matrix. After release, the exhausted carrier stays intact. Besides first order kinetics, controlled release profiles were obtained (e.g. delayed, prolonged).

Conclusion
In summary, smartFilms® as solid dosage form can be used readily for both oral (in mouth cavity) and peroral (through mouth cavity) delivery with controllable release profiles. smartFilms® are a simple way to generate and preserve the amorphous state of active ingredients. Compared to conventional oral film systems, smartFilms® have advantages such as cost-effectiveness, superior absolute and relative loading and reduced stress exposure on the ingredients during manufacturing. Customized cellulose based carriers for smartFilms® can also be produced with 3D printing or electrospinning. smartFilms® are a simple film technology being industrial feasible (film loading like printing a newspaper), but are also suitable for personalized application. In drug stores, patient-tailored smartFilms® can be made by simple variation of the loading volume, loading concentration or the carrier size.