THE MARKET FOR MEDICATED CHEWING GUM

Medicated chewing gum has gained increasing acceptance as a drug delivery system since the first medicated gum product, Aspergum® (acetylsalicylic acid), was launched commercially in 1928. In 1991 the European Pharmacopoeia defined the intended use of medicated chewing gum as the local treatment of mouth diseases or for systemic absorption through the oral mucosa or from the gastro-intestinal tract.¹

Medicated chewing gum has become the first choice for nicotine replacement therapy and over the past decades the perception of chewing gum drug delivery systems has changed from cautious scepticism to general appreciation. Today, several active pharmaceutical ingredients are available in medicated gum formulations.

Most medicated chewing gum products are launched as line extensions to existing OTC medications. The format is often chosen by category managers not because of its pharmacokinetic properties but because chewing gum is easily recognised by consumers and stands out from all the common formats such as lozenges and chewable tablets.

ALKALON’S BUSINESS MODEL

Alkalon’s first product was a generic nicotine gum based on an extrudable gum base. The development work was completed in 2011 and Alkalon received regulatory approval for a portfolio of the gums (2 mg and 4 mg nicotine with various flavours) in a number of European countries. Commercial launch is anticipated by the end of 2012.

The company managed to complete development, up-scaling, bioequivalence and stability studies as well as pan-European registration in less than 30 months, an achievement which was possible only because overall responsibility for all disciplines was kept in-house at Alkalon. The organisation is small and flexible, and the company can easily draw on expertise in regulatory affairs, clinical trials, analysis and other areas, not just from the company’s own advisory board but also from closely connected partner companies with whom Alkalon has worked for many years.

The company’s development laboratory is equipped with all the machinery needed to develop medicated chewing gum formulations based on various technologies, and its technical staff have comprehensive and in-depth experience in the field.

Alkalon currently focuses on the development of line extensions and the continued marketing of its own product portfolio, and is also managing several formulation development projects for large pharmaceutical companies on a contract development basis.

The competitive advantage of Alkalon is not just technology driven. The company is able to compete with Big Pharma through a large number of licensing and supply agreements with generic companies across the world. Pooling the demand from several companies who use new distribution channels for own-label or own-brand products enables Alkalon to supply products at competitive prices.

Alkalon is currently the only independent contract development company with a proven track record which focuses entirely on medicated chewing gum.
SOURCING OF MEDICATED CHEWING GUM

Medicated chewing gum can be manufactured by extrusion or tableting, but until recently only extruded gums have had an acceptable texture and release profile, and all the major nicotine gum brands on the market are still extruded gums.

Manufacturing extruded gums requires highly specialised equipment and, as the market for medicated chewing gum is relatively small, very few CMOs were available until recently. However, the quality of compressible gum bases has increased significantly in the last few years, and today it is possible to manufacture very good tableted gums.

From a sourcing perspective, this has increased the pharmaceutical companies’ freedom to choose CMOs because compressed gums can be manufactured using any tableting machine.

Nonetheless, finding technical staff with sufficient experience in pharmaceutical gum manufacturing remain a challenge.

WHERE TO USE MEDICATED CHEWING GUM

New oral drug delivery systems often compete on fast onset of action and ease of administration.

Medicated chewing gum offers a number of advantages. Importantly, these advantages are not limited to instances where a local effect in the oral cavity or throat are required, where the advantages are obvious, but also apply in systemic delivery applications.

In general, medicated chewing gum is good for convenient administration on demand. There is no need for water and, unlike for example taking tablets or using an inhaler, chewing a piece of gum is not readily associated with illness. Gum is also an obvious choice for children and patients who have difficulty swallowing tablets.

Chewing gum has advantages for the systemic delivery of substances that readily cross the oral mucosa. This provides rapid onset of action and avoids first-pass metabolism and breakdown in the gastro-intestinal tract.

The dissolution rate can be controlled via the quantity and type of gum base in the formulation, as illustrated in Figure 1, making medicated gum suitable for controlled drug release.

The safety of a drug formulated as chewing gum is high, as extreme doses can be ingested only by chewing extensively. The release of drug from the gum if swallowed is very low.

Figure 1: Release of nicotine over time from chewing gum formulations with various contents and types of gum base.

The taste must be appealing and there are a number of ways of masking the unpleasant taste of an API, although extremely bitter drug substances or high dosages might be difficult to work with. Very fat-soluble active ingredients might have such a low dissolution rate that use of a chewing gum formulation is not possible.

Medicated chewing gum is ideal for:
- Nicotine replacement therapy (NRT)
- Treating pain and inflammation in the mouth and throat
- Gastro-oesophageal reflux disease (GORD)
- Prophylaxis of tooth decay
- Buccal absorption of drugs

PRODUCT DEVELOPMENT

The development of a medicated gum formulation from first lab trials to product launch can be described in terms of the phases shown in Figure 2.

Feasibility Study

Development Trials, Lab.

Up-Scaling Trials

Dossier Batch Manufacture / Dossier Compilation / Bioequivalence Study

(Filing)

Registration Process

[Approval]

Launch

Figure 2: Stages of a typical development project at Alkalon.

being a small company Alkalon is able to maintain an overview of the project in its entirety, from the start of the feasibility study to filing. This makes it possible to compile all relevant technical data for the registration file in parallel during the development and upscale phases, resulting in a very fast and flexible process. In a recent case, Alkalon succeeded in writing the registration dossier in seven months while the bioequivalence study and the ICH stability study were performed, and had it ready for filing just one month after receiving the last clinical data and six-month stability data.

Alkalon works in close collaboration with industry experts who have the widest experience of the development and full-scale production of both extruded and compressed gums. By working with Alkalon, its customers gain access to this strong network of experts, which ensures that a new medicated gum project’s progress through development, up-scaling and registration is rapid and unproblematic. Alkalon offers a one-stop shop as a medicated chewing gum solutions provider (see Figure 3).

FEASIBILITY STUDY

When a new development project is started at Alkalon, an initial feasibility study is performed. This provides valuable information at an early stage about important properties such as taste, dissolution and stability of the API in the gum formulation. This is done using a simple test setup and early prototypes to understand the most relevant results quickly and at low cost. A feasibility report can be completed in 6-8 weeks.
The report provides the relevant technical information about possible challenges in the further development and forms a solid basis for a go/no-go decision.

In Alkalon’s in-house development laboratory all relevant equipment for the production of medicated chewing gum samples is available for both extruded and compressed products. The most important analyses can also be performed in-house, which makes it possible to move the project forward in the minimum amount of time.

An internal tasting panel of trained tasters can be expected.

The stability of a medicated gum formulation can also be improved by choosing the right excipients. Screening of the compatibility of the API and the relevant flavours and gum bases is advisable, since these are potentially the most aggressive ingredients. It is an advantage for the stability of a chewing gum formulation that it contains no water. The stability of a gum product can be improved by adding a coating layer, as with a regular tablet.

The dissolution rate of the API will depend on its solubility: the more water soluble it is, the faster it is released. If the drug substance has poor solubility, release can be improved by choosing the right type of gum base, reducing the amount of gum base and by adding a solubiliser.

As discussed here, chewing gum can be produced by two different techniques, extrusion or compression, and the choice of technique also plays a major role as regards taste, dissolution and stability. The traditional method of producing chewing gum is by mixing at approximately 50-60°C, then extruding, rolling and scoring gum cores and subsequently adding a coating layer. In recent years, new techniques of producing compressed gum tablets based on a directly compressible gum base powder have been optimised and today gum products manufactured by compression virtually equal extruded gums in quality.

A compressed gum can offer faster release than extruded gum and, by formulating a two-layer gum tablet and adding the API in the layer without the lipophilic gum base, release can be increased still further if necessary.

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REFERENCE


ABOUT ALKALON

Alkalon is an independent, privately-owned contract research and product development company based in Denmark. The company specialises in the development of medicated chewing gum formulations and is working in partnership with pharmaceutical companies on dosage form development projects and the supply of finished products. Alkalon’s in-house R&D activities take place in a small non-GMP laboratory and all non-core activities are outsourced.

The company has recently developed and registered a portfolio of new, improved nicotine polacrilex chewing gum and is currently the only company which offers licensing and the supply of high quality nicotine gums to the generics industry in Europe and elsewhere.
Test your product in a Medicated Chewing Gum formulation

Alkalon offers to prepare prototypes and a technical report which will give you valuable information about properties, release, and stability of your molecule in a medicated chewing gum formulation.

Meet our team at the CPhI
Finished Dosage
Zone Booth 9A08

Alkalon is a Scandinavian company specialised in formulation development and supply of medicated chewing gum. The company has recently received EU regulatory approval of a new portfolio of nicotine gums.