

# Exploring the world of medicated and functional chewing gum

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Medicated and functional chewing gum is still a relatively novel format in oral delivery systems compared to for instance tablets, liquids and chewable tablets for over-the-counter and nutraceutical products. The use of gum, however, is fast making its way into a variety of applications due to its wide consumer appeal and suitability for a wide range of active pharmaceutical and nutraceutical ingredients.

Spurred by the emergence of nicotine chewing gum in the 1980s, chewing gum continues to be the object of intensive research and development to further explore its potential as a delivery format. At the same time, people are increasingly concerned with improving their health and embracing the concept of active nutrition, where chewing gum has proved to be a popular format.

This paper explains the benefits of chewing gum as an oral delivery format in the light of consumer preferences and new formats, notably bi-layered, compressed gum for formulation of active ingredients.



For thousands of years, people have chewed gum-like, natural substances like tree resin, grasses, leaves and waxes.

In the 1870-80s, flavours and sugar were added to the gum to enhance the taste and gain wider appeal.

In the 1950s, sugar-free gum was invented in response to consumer focus on health, and the first medicated chewing gums saw the light of day.

Since then, a still wider range of active ingredients have found their way into chewing gum.



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## How does chewing gum appeal to consumers?

Today, consumers are facing a large number of different formats, when taking OTC and nutritional products. The list includes tablets, capsules, sachets, gummies, chewable tablets, lozenges, sprays and liquids to name just a few.

Despite the wide range of different dosage formats, it is a well-known fact that consumers may fail to comply with the treatment or health scheme due to dislike of the specific dosage format or lack of trust in the efficacy of the delivery system.

In most markets, chewing gum has become a well-known, socially accepted, portable and discrete format that provides a stimulating experience. Functional medicated chewing gum, however, is a relatively new delivery format, which made its first major breakthrough with nicotine gum in the 1980s. Backed by the strong heritage in the confectionery market, the interest in gum for therapeutic purposes has since accelerated to meet consumer preferences. By 2023, the global functional chewing gum market is expected to reach USD 2.2 billion with annual growth rates of about 4%<sup>1</sup>.

Middle-aged adults present a special opportunity for promoting the use of chewing gum as delivery format. On the one hand, they represent a generation acquainted with the sensorial experience of chewing gum; on the other hand, they consume a large part of the medicines delivered in oral formats. Difficulties swallowing, also known as dysphagia, and dry mouth syndrome, also known as xerostomia, are common ailments among this age group. As chewing gum stimulates the salivary glands, it provides an ideal alternative for delivery of active ingredients to people suffering from dry mouth and difficulty swallowing.

### FACT BOX

#### Benefits of medicated/functional chewing gum

- Promotes high compliance<sup>3</sup>, as consumers consider gum easy, pleasurable and convenient.
- Familiar format, known from the confectionery industry.
- Fast delivery of active ingredients suitable for buccal absorption
- Wide load range to accommodate different APIs and doses.
- Freshens the breath instantly by moistening and refreshing the mouth and throat.
- Promotes good oral hygiene and can help prevent tooth decay by increasing the flow of saliva.
- Counteracts dry mouth or xerostomia by stimulating saliva secretion.
- Convenient and discreet dosage form on the go.
- Helps support a healthy lifestyle with only few calories per serving<sup>4</sup>.

### CASE

## Can chewing gum make a difference for cancer patients?

About one fifth of head and neck cancer patients suffer from dry mouth during and after radiation treatment. Dry mouth may seriously affect dental health and the quality of life of patients, and the oncology department at Odense University Hospital carries out several research projects to ease the late complications of radiation therapy.

A 2018 PhD thesis<sup>2</sup> comprising 91 patients suffering from late complications of radiation treatment analysed the potential of gum to ease symptoms of dry mouth, as the chewing of gum was seen to increase the salivary flow rate and reduce the viscosity of the saliva significantly.

Fertin Pharma developed and patented a unique chewing gum variant based on highly specific requirements for the study. Since patients with dry mouth are highly sensitive to taste, the flavouring of the gum was toned down to a mild taste. The gum base used was softer than ordinary gum to make it easy to chew even with the reduced amount of saliva, which is found in this patient group.

The clinical study clearly showed the potential of gum to ease the symptoms of dry mouth and improve the quality of life for the patients. Chewing gum increased the salivary flow rate and reduced the viscosity of the saliva significantly. Patients, who were part of the trial, reported a significant reduction in symptoms of dryness and experienced improved quality of life on a range of specific parameters.



## When is chewing gum the right delivery platform?

The first experiments of using chewing gum to deliver active substances date back to the 1950s, but the big breakthrough came with the launch of nicotine gum in the early 1980s. Since then, developments have accelerated, and today, new formulations and novel formats are continuously brought to the market for e.g. oral care, digestive health, vitamins and dietary supplements, allergy, painkillers, and energy management to name a few of the application areas. After 40 years, nicotine still tops the list of active ingredients, but several other products in the OTC and nutritional product categories are offered in the market in form of chewing gum. Examples of these actives include caffeine, calcium carbonate, vitamins and even cannabinoids.

During the formulation and design of medical or functional chewing gum, the raw materials of the gum can have different interactions with the formulation. It is therefore critical to balance each of the raw material ingredients of the gum in order to achieve the desired effect and mouthfeel to work with the active ingredient. The basic raw materials included in the manufacturing of chewing gum are: gum base, sweeteners, fillers, softeners, flavours and colours (natural or artificial), enhancers such as buffer systems and anti-oxidants.

In general, chewing gum works best for delivery of water-soluble ingredients, which can be released rapidly and completely within the desired timeframe as the gum dispenses the active ingredient into the oral cavity whilst chewing. Through the right design of the formulation, insoluble actives might be handled effectively in chewing gum formats as well. The active ingredients in chewing gum can be targeted to act locally, e.g. for treatment of mouth sores or mouth dryness, or to act systemically through the oral mucosa.

The local and systemic efficacy of chewing gum was analysed in a study of more than 4,000 Americans aged 12 to 55, who were asked about their gum chewing habits. The study showed that the average chewing time was 36 minutes, which is sufficient time to achieve both local effect in the oral cavity or buccal absorption for systemic effects<sup>5</sup>.

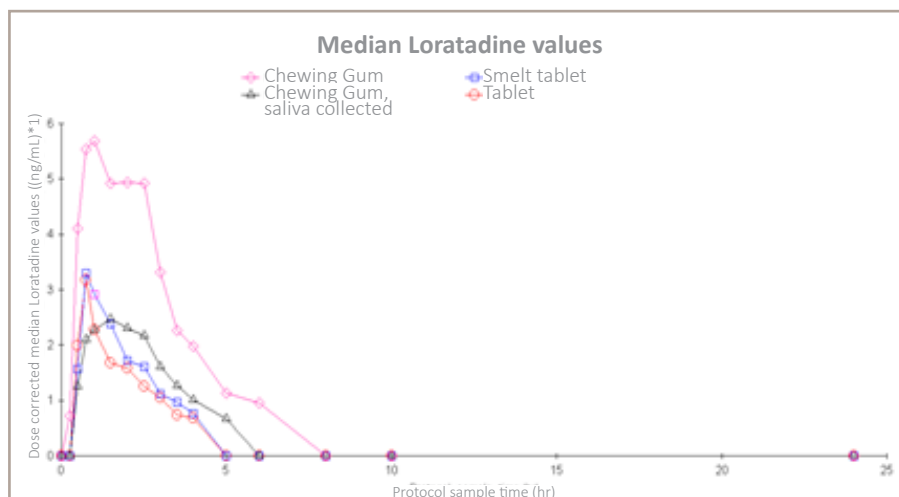


Figure 1: The figure shows the advantages of chewing gum as a drug delivery format with fast and prolonged action. In this case with the active Loratadine (antihistamine). The study performed by Fertin Pharma showed best utility of the API with chewing gum and approx. 40% buccal absorption from chewing gum.

When active ingredients are absorbed directly via the buccal membrane, they bypass the digestive system, which means that the dosage can be reduced compared to other oral drug delivery formats. The release rate can be carefully controlled through the formulation of the gum, also allowing sustained release in the oral cavity.

Chewing gum provides a safe delivery of active substances, which are released by chewing and dissolved in saliva. It is important to note that part of the active substance is swallowed with the saliva when chewing gum and hence absorbed through the gastrointestinal tract just like tablets. The fact that the active substance is dissolved first in saliva means that the absorption takes place faster in the gastrointestinal tract.

### FACT BOX

#### When to choose functional chewing gum?

The following actives have been proved to be highly effective in chewing gum formats:

- Nicotine
- Cannabinoids
- Vitamins and dietary supplements
- Oral care
- Energy management (e.g. caffeine)
- Pain killers
- Allergy
- Cough and cold
- Gastrointestinal, reflux
- Sleep and relaxation



As mentioned before, chewing gum is a highly effective delivery format for water-soluble ingredients, whereas fat-soluble ingredients such as vitamins E, A and D can be more difficult to release from gum. To address this problem, the fat-soluble active ingredients can be added to the mint layer of bi-layer compressed chewing gums to prevent the active ingredient sticking to the gum base.

## New opportunities with bi-layered products

New technologies continuously evolve to provide consumers with convenient and pleasurable formats for OTC products and nutraceuticals. One of the developments is the direct compression process, which is used for sensitive actives that are not suitable for extruded gum products whose processing involves intensive mixing and elevated temperatures.

The bi-layer format offers effective separation of the active ingredients and can therefore deliver ingenious combinations of actives with, for instance, different release times and absorption in the mouth, throat or later in the gastrointestinal tract. The right dosage is precisely controlled in each layer of the compressed gum to obtain maximum safety and efficacy of each API.



In tests, consumers have expressed a strong liking for the combination of the crunchy, fast-dissolving mint and the long-lasting gum. Especially for young adults, the bi-layered gum has shown attractive potential as an efficient delivery platform for OTC and nutritional products in the consumer healthcare category.

A 2019 survey carried out by Fertin Pharma in North America asked 200 participants to describe their experiences with different formats throughout its life-cycle, from first seeing the product to ingesting it and disposing of it (Fig 2). The study showed that 80% of participants expressed a high degree of liking for the compressed chewing in all stages of the product's life cycle.

Why do most age groups like chewing gum so much? When looking into the 2019 Fertin consumer survey, a number of reasons are stated, for example that chewing gum is characterized as a discrete and convenient dosage form, which can be consumed anywhere and anytime without water and provides a fresh breath. Furthermore, chewing gum is considered an enjoyable delivery format, which provides a pleasurable and long-lasting experience stimulating the senses.

### FACT BOX

The bi-layered compressed chewing gum typically contains a gum layer and a mint layer. The mint layer dissolves fast, releasing the active substances within the first chews. The gum layer on the other hand, offers a prolonged release of the active during the entire chewing period.

When using the direct compression process in gum manufacturing, all ingredients are dry and no heating takes place. The gentle process at ambient temperature protects the active substances and accommodates a wide range of APIs.

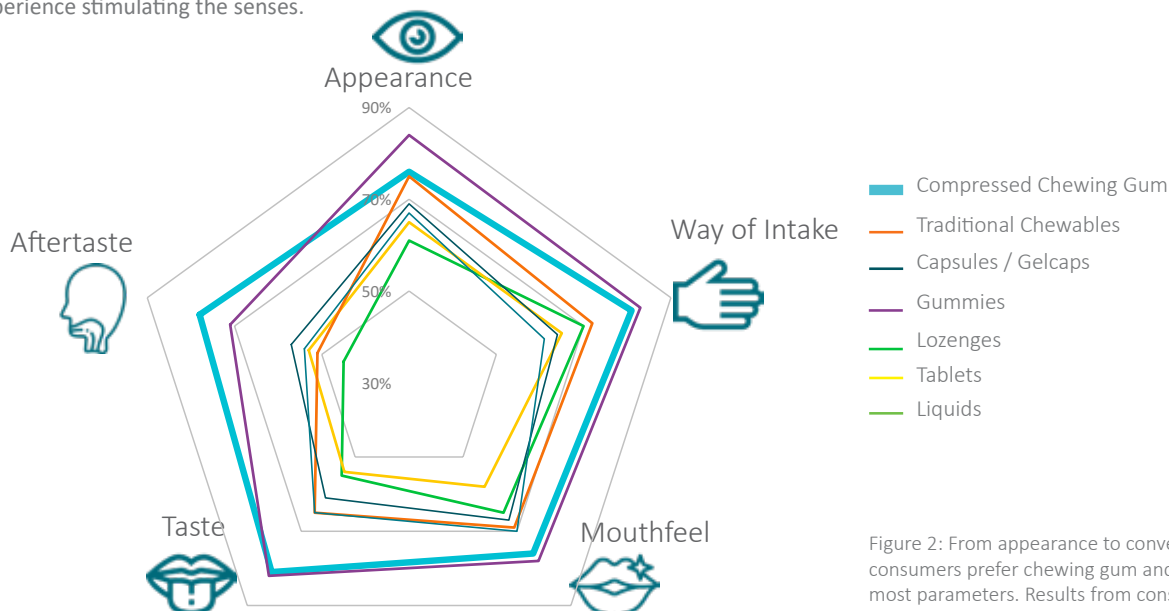
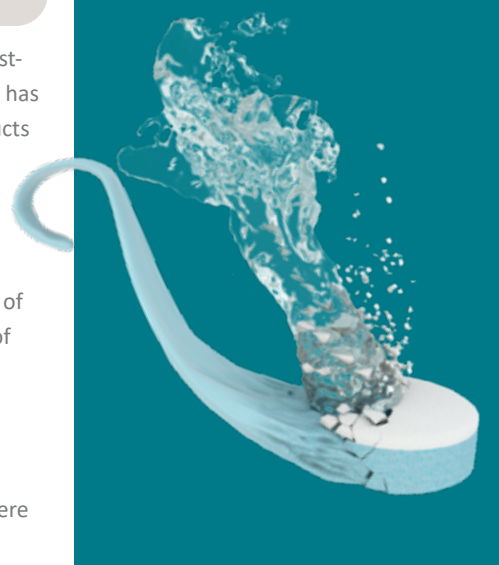




Figure 2: From appearance to convenience and taste, consumers prefer chewing gum and gummies on most parameters. Results from consumer survey carried out by Fertin Pharma in USA, August 2019.

Extruded gum	Compressed, bi-layer gum
 <p>Intensive mixing, forcing materials into a continuous matrix</p>	 <p>Gentle mixing, powders mixed together in tumbler; materials mixed at solid state</p>
Process temperature approx. 50°C; mass is partially liquefied	Process temperature at ambient conditions; allows more APIs, also sensitive ingredients like vitamins and probiotics
Homogeneous mix with both gum base and API; API uniformly dispersed in gum matrix	Two separate layers that can contain the same API or two different
Surface covered by coat layer	Tablet like surface
Risk of incomplete release of certain active ingredients and potential reaction over time between API and other ingredients	Risk of API damage due to exposure to ambient air. Moisture may affect appearance and color



## The art of taste masking

The taste of orally dispensed OTC and nutritional products is extremely important for patient compliance and motivation. The problem is, however, that most APIs have an unpleasant taste, and the issue of taste is further complicated by the fact that taste is a highly subjective experience and varies from one age group or culture to the next.

Taste masking and the science of developing products with better mouthfeel are therefore major focus areas in the research and development activities related to oral dosage formats. This is especially important in chewing gum, which tends to stay longer in the mouth than other, more traditional tablets and capsules. Taste masking is therefore critical when developing user-friendly chewing gum.

Unfortunately, there is no universal solution to taste masking, since every API presents unique challenges. It is a trial-based process of testing different flavours ranging from classic mint and menthol to coffee, berries, vanilla and cinnamon, and drawing on profound knowledge of taste masking and taste preferences in particular user groups, e.g. elderly people, children and youth as well as varying national food culture traits.

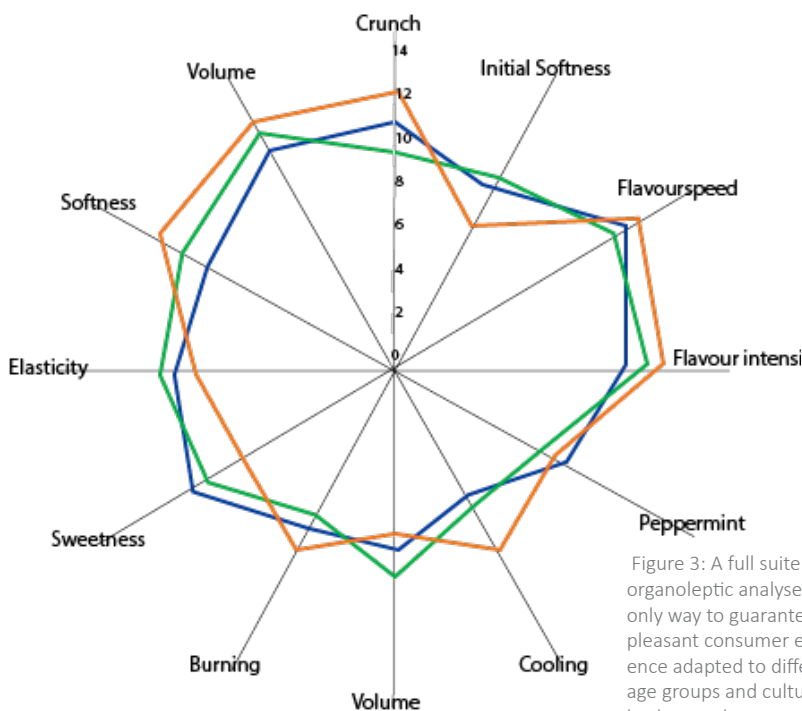


Figure 3: A full suite of organoleptic analyses is the only way to guarantee a pleasant consumer experience adapted to different age groups and cultural backgrounds.

### CASE

## Gum with calcium carbonate relieves heartburn better

Chewing gum is a highly effective delivery format for heartburn relief. Gum provides immediate relief and sustains the effect over a longer period than chewable tablets, up to two hours.

The good effect of chewing gum can be explained by several factors, among others increased saliva flow and the rate of swallowing. Studies have shown benefits associated with calcium carbonate's antacid properties by decreasing heartburn and indigestion neutralizing stomach acids<sup>1</sup>). Calcium carbonate gum effectively neutralizes esophageal acidity and relieves symptoms following a meal. It is superior to chewable antacids in terms of the duration of heartburn relief<sup>6</sup>.

#### Benefits of Antacid Chewing Gum

- Convenient and discreet
- Fast onset of action to relieve acid indigestion and heartburn
- Sugar-free
- Cool and refreshing mint flavor helps getting rid of the bad taste in the mouth

## CASE

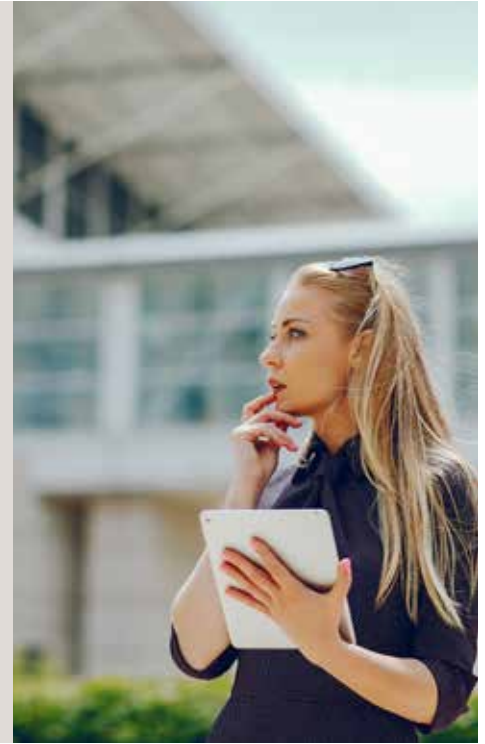
# Increased energy and alertness through caffeinated chewing gum

Caffeine which exists in drinks such as coffee as well as in drug dosage forms on the global market is among the materials that increase alertness and decrease fatigue. Compared to other forms of caffeine products, caffeine gum can create faster and more prominent effects.<sup>7</sup>

Fertin's patented energy and alertness products contain energy stimulating active ingredients such as caffeine and B-vitamins. They may be marketed either as dietary or food supplement, depending on local regulations.

Benefits of Energy & Alertness Chewing Gum:

- Easy to use, without the need for water
- Suitable for people who have difficulty swallowing
- Rapid onset of action
- Lesser side effects because the active substances are absorbed buccally without passing through the primary hepatic metabolism
- Less risk of overdosing



## The sky is the limit

The acceptance of medicated and functional chewing gum is growing year by year. The industry is maturing, consumer interest is growing and the convenience and therapeutic benefits related to chewing gum spark new developments. Chewing gum stands out as one of the fast growing, innovative categories supported by its convenience, efficacy, familiarity and not least its pleasurable mouthfeel.

Nevertheless, the innovation potential of compressed, bi-layered gum is far from fully discovered. In fact, the technology is still in its early phases with multiple experiments combining different components, APIs and gum bases. So far, it is possible to combine two or three active ingredients, but the future is likely to see more combinations and even brand new formulations that support a healthier and active lifestyle.

There are endless variables on the journey from the first idea to the final product, and they all play a vital role in achieving a successful product launch with wide consumer appeal. The iterative process to discover the right gum base, API stability and controlled API release, thickness of mint and gum layers, chewing robustness and other important factors before market release is best performed in close collaboration between R&D specialists, the customer and manufacturing artisans.

We are only at the beginning and the future will see on-going development with new drugs, new formats and more API combinations. Among some of the emerging applications are cannabinoids and a multitude of nutraceuticals and OTC products, where chewing gum is proving to be a popular alternative to more traditional tablet formats.

It may be difficult to imagine that a small piece of chewing gum contains this kind of innovation potential, but the development of medicated and functional gum is likely to continue to grow in the coming years.

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# Your one-stop-shop for innovative dosage formats



Fertin Pharma is a Contract Development and Manufacturing organization (CDMO) with headquarters in Denmark, specializing in innovative oral and intra-oral dosage formats with nutraceutical and pharmaceutical ingredients, aimed to give a pleasurable experience to consumers.



Consumer Insights



Quality control & Assurance



Research & Development



Manufacturing & Packaging



Sensory Optimisation



Intellectual Property



Regulatory & Compliance

## Consumer-friendly technologies

Our versatile dosage formats are designed to provide a convenient and pleasurable intake of pharmaceutical and nutraceutical products. Most consumer healthcare areas and age groups can be targeted based on their needs, preferences and behaviours:

Immune Support · Vitamins and Dietary Supplements · Oral Care · Energy Management · Cough and Cold · Allergy Care · Nicotine Replacement Therapy · Cannabinoid Applications · Digestive Health · Pain Management ...and many others

### ZAPLIQ® CHEWABLE TABLET

The next generation of chewable tablets

- Easy to swallow as a sip of water
- Unique mouthfeel
- Excellent taste-masking properties
- Wide range of flavours, colours, textures and shapes



### COMPRESSED CHEWING GUM

Controlled release of active ingredients

- Allows separation of sensitive actives
- Soft and chewable texture
- Wide range of flavours, colours, textures and shapes
- Excellent taste-masking properties



### POWDER

Provides new mouthfeel experiences. Can be used by mixing in water or directly in the mouth



### EXTRUDED GUM

High quality chewing gum, based on decades of confectionery and pharmaceutical experience



### LOZENGE AND FDT

Fast or slow dissolving compressed tablets for a controlled release



## Why choose Fertin Pharma as your CDMO of innovative dosage formats?



### Heritage

Fertin creates effective products with a pleasant taste and mouthfeel, building on 100 years of history in chewing gum and more than 30 years' pharmaceutical experience.



### Quality

We ensure reliable and consistent quality in every product leaving our facilities. Our manufacturing facilities and standard production routines comply with the rigid cGMP (current Good Manufacturing Practice) and the highest EU standards.



### Proven Track Record

Fertin works with leading global brands as well as store labels. Our products are used by consumers all around the world.



### Innovation & Uniqueness

Fertin products are developed based on consumer insights and protected by a strong portfolio of patents. We have been granted more than 100 patents, including some regarding taste masking and release profiling.