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Review Article

# A BRIEF REVIEW ON MEDICATED CHEWING GUM'S

**Saloni Jain*, M.P.Khinchi, S.P. Singh, Nitin Nama, Narendra Gauttam**

Department of Pharmaceutics, Kota College of Pharmacy, Kota, Rajasthan, India

***ABSTRACT***

*The present invention is directed to chewing-gum preparations which are particularly useful for treating gastroesophageal reflux disease. Typically, the chewing-gum preparation comprises a chewing-gum base and more than one ingredient selected from the group consisting of an acid neutralizing agent, an anti-gas agent, and an acid production inhibitor, and desirably all three ingredients.*

***Keywords :*** *Chewing-gum, Gastroesophageal, Acid neutralizing agent, Ingredient.*

## INTRODUCTION

Medicated Chewing Gum is a Novel Drug Delivery System (NDDS) containing masticator gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. Medicated Chewing Gum is a "Delivery system" are intended to introduce medicated substances into the saliva and thus into the blood stream faster than pills.

Medicated Chewing Gum is considered as Vehicle or a Drug delivery system to administer active principles that can improve health and nutrition. has a proven value as a delivery vehicle for Pharmaceutical and Nutraceutical ingredients. It can be taken discreetly without water and allows for local and systemic delivery.

It can be employed for treatment of diseases of the oral cavity and throat, e.g. for caries prevention, or it can release drugs that can be absorbed through oral mucosa directly into the systemic circulation.

*Corresponding author:*
**Saloni Jain*
*B.Pharm Kota College of Pharmacy, Kota, Rajasthan, India*
*E mail: jainsaloniak@gmail.com*
*Mobile. - 8741876405*

In addition, drug that is not absorbed by the oral cavity membranes can be dissolved in the saliva before swallowing, thus leading to a more rapid onset of action.

Pharmacological Active Agents or Drugs are formulated into variety of dosage forms like Tablets, Capsules, Injectables, Inhalers, Ointments etc considering Physicochemical properties, Pharmacokinetic & Pharmacodynamic parameters and Biopharmaceutical aspects of Drugs. Today Medicated Chewing Gum is convenient drug delivery system which is appropriate for a wide range of active substances.

Many therapeutic agents are absorbed in the oral cavity. For the drugs having significant buccal absorption, dosage form such as permits more rapid therapeutic action compared to per-oral dosage forms.

### MERITS OF MCG'S:[1,6,7]

- Dose not requires water to swallow. Hence can be taken anywhere.
- Advantageous for patients having difficulty in swallowing.
- Excellent for acute medication.
- Counteracts dry mouth, prevents candidiasis and caries.

- Highly acceptable by children.
- Avoids First Pass Metabolism and thus increases the bioavailability of drugs.
- Fast onset due to rapid release of active ingredients in buccal cavity and subsequent absorption in systemic circulation.

**DEMERITS OF MCG'S:[8]**

- Risk of over dosage with MCG compared with chewable tablets or lozenges that can be consumed in a considerable number and within much shorter period of time.
- Sorbitol present in MCG formulation may cause flatulence, diarrhea.
- Additives in gum like flavoring agent, Cinnamon can cause Ulcers in oral cavity and Licorice cause Hypertension.
- Chlorhexidine or mucosal application is limited to short term use because of its unpleasant taste and staining properties to teeth and tongue.
- Chewing gums have been shown to adhere to different degrees to enamel dentures and fillers.
- Prolong chewing *on* gum may result in pain in facial muscles and earache in children.

**FORMULATION**

Medicated chewing gum is a combination of a water-insoluble phase, known as gum base, and a water-soluble phase of sweeteners, flavoring and sometimes food coloring. is a mixture of natural or synthetic gums and resins, sweetened with sugar, corn syrup, artificial sweeteners and may also contain coloring agents and flavor. The basic raw material for all MCGs is natural gum Chicle, obtained from the sapodilla tree[9]. Chicle is very expensive and difficult to procure therefore other natural gum or synthetic materials like polyvinyl acetate and similar polymers can be used as gum base.

Typically Chewing Gum comprises two parts:

- Water- insoluble chewable gum base portion.
- Water-soluble bulk portion.

**Water-insoluble chewable gum base portion:**

Gum base is the non-nutritive, non-digestible, water-insoluble masticator delivery system used to carry sweeteners, flavors and any other desired substances in . It provides all the basic textural and masticator properties of gum. Generally comprises Elastomers, Resins, Fats and Oils, and Inorganic fillers.[4,10] Old gum bases were based on either natural elastomers such as latexes, vegetable gums like chicle, spruce gum, and mastic gum, or alternatively on waxes, e.g. paraffin wax and beeswax, but today synthetic rubbers are preferred. Gum bases for are different than those for bubble gum. A bubble gum base is formulated with the ability to blow bubbles. Contains 20-25% gum base and sugar-free chewing gum contains 25-30% gum base.

***Elstomers:***

Elastomers provide elasticity or bounce, controls gummy texture, and can be:

**Natural Elastomer:**

Natural rubbers like Latexes (e.g. couma macrocarpa (also called leche caspi or sorva). loquat (also called nispero), tunu, Natural gums such as jelutong, Caspi, Perillo or chicle which is still commercially produced)

**Synthetic Elastomer:**

Rubbers (e.g. styrene-butadiene rubber,butyl rubber, polyisobutylene).


**Figure:-1 Synthetic Elastomer**

**A is a schematic drawing of an unstressed polymer. The dots represent cross-links. B is the same polymer under stress. When the stress is removed, it will return to the A configuration.**

**Plasticizers:**
These are used to regulate cohesiveness of product. These are again divided into Natural and Synthetic.

**Natural Plasticizers:**

Include Natural rosin esters like Glycerol Esters or partially hydrogenated Rosin, Glycerol Esters of Polymerized Esters, Glycerol Esters of Partially dimerized Rosin & Pentaerythritol Esters of Rosin.

**Synthetic Plasticizers:** Include Terpene Resins derived from a-pinene and/or d-limonene.

**Fillers or Texturizers:**

Provide texture, improve chew ability, and provide reasonable size of the gumlump with low dose drug. Commonly used fillers are Magnesium and Calcium Carbonate, Ground Limestone, Magnesium and Aluminium Silicate, Clay, Alumina, Talc, Titanium Oxide & Mono/ di/ tri Calcium Phosphate.

**Water-soluble bulk portion:**

Contains Bulk Sweeteners, High intensity Sweeteners, Flavoring agents, Softners, Emulsifiers, and Colors & Antioxidants.

**Softeners and Emulsifiers:**

These are added to the chewing gum in order to optimize the chewability and mouth feel of the gum. Softeners include Glycerin, Lecithin, Tallow, Hydrogenated Tallow, Mono/ di/ tri-Glycerides, Fatty acids like Stearic acid, Palmitic acid, Oleic acid and Linoleic acid.

**Colourants and Whiteners:** A food coloring is any substance that is added to change its color.

**Natural food dyes**

- Caramel coloring, it is made from caramelized sugar.
- Annatto is a reddish-orange dye made from the seed of a tropical tree.
- Beet juice, turmeric, saffron, paprikas are also used as colorants.
- Titanium dioxide occurs naturally in minerals.

**Artificial food dyes**

In the USA, the following artificial colorings are permitted:

- FD&C Blue No.l - Brilliant Blue FCF, El33 (Blue shade)
- FD&C Green No.3 - Fast Green FCF, E143 (Bluish green shade)
- FD&C Red No.3 - Erythrosine, El27 (Pink shade)
- D&C Yellow No.6 - Sunset Yellow FCF, El 10 (Orange shade)

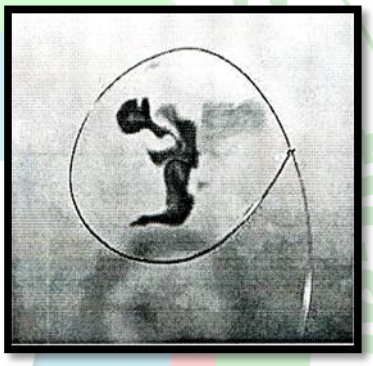

**Figure:-2 Food coloring spreads on a thin water film.**

**Sweeteners:** These are of three types:

- Aqueous Sweeteners.
- Bulk Sweeteners.
- Sugar Substitutes.

**MANUFACTURING PROCESS**

The gum base is melted at a temperature of about 115 °C (240 °F), until it has the viscosity of thick maple syrup, and filtered through a fine mesh screen. Then it is further refined by separating dissolved particles in a centrifuge, and further filtered. Clear base, still hot and melted, is then put into mixing vats.

Other ingredients that may be added include: Powdered sugar, whose amount and grain size determines the brittleness of the result, corn syrup and/or glucose which serve as humectants, coat the sugar particles and stabilize their suspension, and keep the gum flexible, various softeners, food colorings, flavorings, preservatives and other additives.

The homogenized mixture is then poured onto cooling belts, and cooled with cold air. Extrusion, optionally rolling and cutting, and other mechanical shaping operations follow. The chunks of gum are then put aside to set for 24 to 48 hours. Coated chewing gums then undergo other operations. The chunks are wrapped with optional undercoating for better binding with outer layers then immersed into liquid sugar. The pellets are then colored and coated with a suitable glazing agent, usually a wax.

Different methods employed for the manufacturing of MCG can be broadly classified into three main classes namely.

- Conventional/ Traditional Method (Melting).
- Freezing, Grinding and Tabletting Method.
- Direct Compression Method.

**Conventional/ Traditional Method:**

Components of gumbase are softened or melted and placed in a kettle mixer to which sweeteners, syrups, active ingredients and other excipients are added at a definte time. The gum is then sent through a series of rollers that form into a thin, wide ribbon. During this process, a light coating of finely powdered sugar or sugar substitutes is added to keep the gum away from sticking and to enhance the flavour. In a carefully controlled room, the gum is cooled for upto 48 hours. This allows the gum to set properly. Finally the gum is cut to the desired size and cooled at a carefully controlled temperature and humidity.

**Freezing, Grinding and Tabletting Method:** [2]

This method has been developed with an attempt to lower the moisture content and alleviate the problems mentioned in conventional method.

**Freezing and Grinding:**

The MCG composition (base) is cooled to a temperature at which the composition is sufficiently brittle and would remain brittle during the subsequent grinding step without adhesion to the grinding apparatus. The temperature required for cooling is determined in part by the composition of the MCG and is easily determined empirically by observing the properties of the cooled chewing gum composition. Generally the temperature of the refrigerated mixture is around -15°C or lower.

**Tabletting:**

Once the coolant has been removed from the powder, the powder can be mixed with other ingredients such as binders, lubricants, coating agents, and sweeteners etc, all of which are compatible with the components of the base in a suitable blender such as sigma mill or a high shear mixer.

**Direct Compression Method:**

The manufacturing process can be accelerated if a directly compressible chewing gum excipient is available. The limitations of melting & freezing can be overcome by the use of these.

PHARMAGUM is one such compactable gum system developed by SPI Pharma. Pharmagum is a mixture of polyol(s) & or sugars with a chewing gum base.

**CHEWING APPARATUS:-**

**Equipment/ Construction:-**

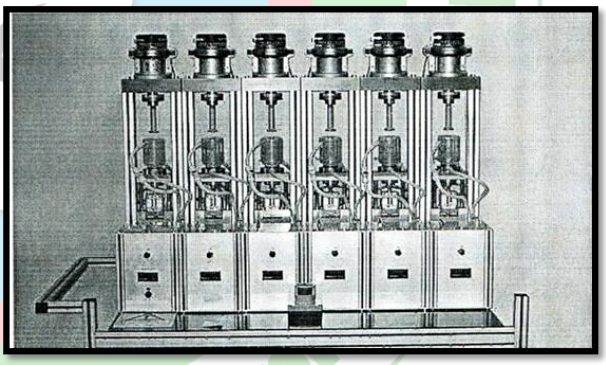

**Figure:-3 Chewing Apparatus DRT**

The most important parts of the chewing apparatus are as follows:

- Revolving device for the upper chewing surface stand.
- Thermostated test cell upper chewing surface (upper jaw).
- Lower chewing surface (lower jaw).
- Device for axial up and down chewing motion.
- Lift
- Electronic control device for chewing frequency, chewing time etc.

- Mobile carrier Water bath.

The chewing equipment is placed on a mobile carrier. The material and the form of the parts that are in contact with the chewing gum are decisive for the function of the apparatus. The material of chewing surface (jaw) is acid proof stainless steel with a blasted surface.

The blasted surface makes the jaws get a good grip of the chewing gum during the mastication. The upper jaw is stationary in relation to the lower jaw and also completely fixed against up and down going movements although it is turning around its axis by a revolving device. The lower jaw is moving up and down by a device for linear/axial chewing movements but is fixed against revolving movements. The test cell follows the lower jaw in its movements.

## IN-VITRO DRUG RELEASE TESTING

***Factors affecting release of active ingredients:***

**Contact Time:**

The local or systemic effect is dependent on time of contact of MCG in oral cavity. In clinical trial chewing time of 30 minutes was considered close to ordinary use.

**Physicochemical properties of active ingredient:**

Physicochemical properties of active ingredient plays very important role in release of drug from MCG. The saliva soluble ingredients will be immediately released within few minutes whereas lipid soluble drugs are released first into the gum base and then released slowly.

**Inter individual variability:**

The chewing frequency and chewing intensity which affect the drug release from MCG may vary from person to person. In-vitro study prescribed by European Pharmacopoeia suggest 60 cycles per minute chewing rate for proper release of active ingredient[6].

**Formulation factor:**

Composition and amount of gum base affect rate of release of active ingredient. If lipophilic fraction of gum is increased, the release rate is decreased[2].

## THERAPEUTIC USES

- The use of sugar free gum to counteract dental caries by stimulation of saliva secretion has led to a more widespread use and acceptance of gums.
- It has been proved that chewing non- s increases plaque pH, stimulates saliva flow and decrease decay.
- MCGs containing Chlorhexidine for treatment of gingivitis and plaque has been available.
- The use of MCG in the treatment of oral infections has also been reported.
- The active ingredient is released from the MCG and sufficient concentration is achieved in the oral cavity to prevent or treat local conditions of oral cavity.
- MCGs are also useful delivery system for agents intended for systemic delivery.
- Drug that is released from MCGs within oral cavity can be absorbed via buccal mucosa.
- The MCGs can also be used as an alternative tool to buccal and sublingual tablets which are intended to act systemically because active ingredient is released more uniformly and cover greater area of absorption in oral diseases.
- Oral diseases are prevented or cured with MCG.

## PATENTS

***Patent Application:*** [42]

**For Composition and Manufacturing Process**

A composition for having the active principle dispersed in the gum and coated by a mixture consisting of a hydrosoluble element and a water insoluble one.

The principle can be one or more from the group consisting of nicotine, ibuprofen, paracetamol, D-metorfan, dimenhydrinate, ginger, 1-ascorbic acid (vitamin C),

acetylcysteine, ephedrine, Dpseudoephedrine, valerian, ranitidine, chlorexidine, tibenzonium iodide, preferalby nicotine while the soluble element is a carbohydrate, preferably sorbitol and the water insoluble element is an oil, preferably hydrogenated castor oil. A process for manufacturing a tablet of having the composition according to the invention is also described. The tablet according to the invention has high stability organoleptic properties and gradual and controlled release properties.
Inventors (Country) : Badetti, Rolando (Italy)
Owners (Country) : Badetti, Rolando (Italy)
Applicants (Country): ATP Avant-Garde Technologies & Product
Marketing & Licensing S.A (Switzerland)
PCT Filing Date : Oct. 18, 1999
PCT Publication Date : Sep. 28, 2000
International Class (IPC): A61K 9/00 (2006.01) A61K 9/68 (2006.01)
Patent Cooperation Treaty (PCT): Yes National Entry: Sep. 20, 2001 PCT Filing number: PCT/EP1999/007917 International publication number: WO2000/056281 Application priority data:

**Table -1- Patent Cooperation Treaty (PCT)**

| Application | Country | Date |
|---|---|---|
| MI99A00057 | Italy | Mar. 22, 1999 |
| 09/387,538 | United States | Aug. 31, 1999 |

**United States Patent:**

**For containing cough suprresing agent**

Patent Issued: December 8, 1998 Inventor: Penny A. Cash Abraham I. Bakal

Assignee: Cumberland Packing Corporation Application No. : 885382 filed on 1997-06-

Current US Class: 424/439, 424/440, 424/441

Field of Search: 424/43, 424/440, 424/441 Examiners: Thurman K Assistant: D Faulkner Attorney, Agent or Firm: Steinberg & Raskin, P.C.

**Description**

The present invention is directed to medicament-containing chewing gum compositions. In particular, the present invention is directed to chewing gum compositions which effectively mask the unpleasant tastes of the medicaments contained therein over extended chewing periods. One of the most popular and effective antitussive agents is dextromethorphan.

**United States Patent:**

Patent Issued: March 25, 2003 Inventors: West; Douglas H. Application No.: 790528 Filed: January 29, 1997

**SUMMARY**

Medicated chewing gum is a Novel Drug Delivery System (NDDS). The Medicated chewing gum compositions includes : A Gum base component; Water soluble sweetener component such as sucrose, sorbitol, xylitol, alone or in combination with intense sweeteners such as saccharin or aspartame, Emulsifier such as lecithin, Plasticizer such as corn syrup, hydrogenated corn syrup, Coloring agents, Antioxidants, Softeners, Waxes; for example, natural and synthetic waxes, Mineral adjuvants such as calcium carbonate, magnesium carbonate, Preservatives: For example, titanium dioxide and other dyes, High intensity sweetener, Flavorant.

The gum base will be present in amounts from about 5% to about 94%, by weight of the final chewing gum composition.

The development costs of new active pharmaceutical ingredients have increased dramatically and pharmaceutical companies are currently intensifying their focus on new initiatives to achieve maximum profit from their products and brands.

A cost effective way to generate increased revenue is line extensions based on new pharmaceutical formulations.

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