

Review Article

A Comprehensive Review On: Medicated Chewing Gum

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Received 16 June 2014; received in revised form 22 June 2014; accepted 22 June 2014

Available online 23 June 2014

Abstract

In recent years scientific and technological advancements have been made in the research and development of oral drug delivery systems. The reasons that the oral route achieved such popularity may be in part attributed to its ease of administration. Chewing gum is one of the very popular oral confectionery products. Now-a-days it is considered to be a potential and convenient modified release drug delivery system which can be used in pain relief medication, smoking cessation, travel illness, freshening of breath, prevention of dental caries, alleviation of vitamin or mineral supplementation etc. Chewing gum known as gum base (insoluble gum base resin) contains elastomers, emulsifiers, fillers, waxes, antioxidants, softeners, sweeteners, food colourings, flavoring agents, and in case of medical chewing gum, active substances. It offers various advantages over conventional drug delivery systems. Unlike chewable tablets medicated gums are not supposed to be swallowed and may be removed from the site of application without resorting to invasive means. An *In-vitro* apparatus was specially designed and constructed for release testing of medicated chewing gums. Medicated chewing gums are excellent mobile drug delivery systems for self-medication as it is convenient and can be administered discretely without water.

Keywords: Oral drug delivery, chewing gum, patient compliance, mobile drug delivery system, mouth diseases.

1. Introduction

Medicated chewing gum is solid, single-dose preparations that have to be chewed & not swallowed; chewing gums contain one or more active ingredient that is released by chewing. A medicated chewing gum is intended to be chewed for a certain period of time, required to deliver the dose, after which the remaining mass is discarded. During the chewing process the drug contained in the gum product is released from the mass into saliva & could be absorbed through the oral mucosa or swallowed reaching stomach for gastro-intestinal absorption. The first medicated chewing gum was introduced in USA 1924 with brand name Aspergum®. However, chewing gum did not gain acceptance as a reliable drug delivery system until 1978, when nicotine chewing gum became available in 1980.

Most of the chewing gum were used for smoking cessation (containing the nicotine) and also used for oral and dental hygiene, motion sickness, and freshening of the breath. In addition, a large number of chewing gum intended for caries prevention, xerostomia alleviation, tooth whitening, and vitamin/mineral supplementation also in market. Chewing gum can be used as drug delivery for many active components. Children in particular may consider chewing gum as a more preferred method of drug administration compared with the oral, liquids and tablets. The use of Medicated chewing gum is feasible in local treatment of diseases of oral cavity as well as treatment of systemic conditions. With the inclusion of medicated chewing gum in the European Pharmacopoeia in 1998, have further contributed to the acceptance of this method of drug delivery. Today, medicated chewing gum meets the same high-quality standards as tablets and can be formulated to obtain different release profiles of active

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substances, thus enabling distinct patient group targeting. Chewable tablets and Chewing Gum permits more rapid therapeutic action compared to per-oral dosage form. In Children particularly may consider chewing gum as a more preferred method of drug administration compared with oral liquids and tablets. It had shown that people chewing gum was better at keeping awake and alert, and that gum chewing eased tension. The anecdotal effect of chewing gum on weight loss has also been studied recently. Though there are many other interesting anecdotal effects that result from gum chewing, such as the easing of blocked ears. It can be used either for local (mucosal) treatment of mouth disease or for systemic (transmucosal) delivery by direct intraoral absorption through the buccal mucosa.

History

Chewing gum has an old and long history, in 50 AD, the Greeks sweetened their breath and cleansed their teeth by using mastiche, a resin from the bark of mastic tree. (The English word "masticate" is derived from the root word mastiche.) At the beginning of its history this product was not so much accepted by the public. The social acceptance of chewing gum, however, has increased dramatically over the years. As chewing gum has become more widely accepted and practiced, songwriters, film makers and authors have incorporated related themes into their works. One thousand years ago, the ancient Mayan Indians of Yucatan chewed tree resin (chicle) from the Sapodilla tree. Spruce gum, which was manufactured in 1848, became the first chewing gum product to be manufactured commercially called "STATE OF MAINE PURE SPRUCE GUM." However, its use was eventually replaced by paraffin, which is still being chewed in some areas. During the 1860's, a New York photographer named Thomas Adams, realized the potential market for chewing gum products. He wrapped pieces of pure, flavorless chicle in colored tissue paper, packaged them in boxes, and left them on consignment with numerous drugstore owners. The gum was named Adams New York No. 1. Public response to the product was very favorable.

The first patent for chewing gum, U.S. number 98,304 was filed on December 28, 1869 by Dr. William F. Sample, a dentist from Mount Vernon, Ohio. This product, consisting of liquorice and rubber dissolved in alcohol and naphtha, was initially intended to be used as a dentifrice. In 1891, William Wrigley Jr., arrived in Chicago with \$32 in cash with a desire to market his special variety of soap. Eventually, he switched from soap to baking powder sales and offered chewing gum premiums to merchants who became his customers. By 1892, when the premiums had become more popular than the baking powder, Wrigley launched his first chewing gum products, LOTTA and VASSAR. A year later, he developed JUICY FRUIT, and shortly thereafter, WRIGLEY's SPEARMINT gum. Sugarless gum made its debut in the early 1950s, generally used sorbitol as a sugar substitute. The first brand to be marketed was Harvey's followed by Trident and Carefree. In 1975, the Wm. Wrigley Jr. Company introduced the arrival of a new chewing gum product, Freedent, designed especially for denture wearers, which did not stick to most dentures as ordinary gum did.

Merits of Medicated Chewing Gum

- 1) Does not require water to swallow. Hence can be taken anywhere,
- 2) Advantageous for patients having difficulty in swallowing,
- 3) Excellent for acute medication
- 4) Counteracts dry mouth, prevents candidiasis and caries,
- 5) Highly acceptable by children,
- 6) Avoids first pass metabolism and thus increases the bioavailability of drugs,
- 7) Fast onset due to rapid release of active ingredients in buccal cavity and subsequent absorption in systemic circulation,
- 8) Gum does not reach the stomach. Hence G.I.T. suffers less from the effects of excipients,
- 9) Stomach does not suffer from direct contact with high concentrations of active principles, thus reducing the risk of intolerance of gastric mucosa,
- 10) Fraction of product reaching the stomach is conveyed by saliva delivered continuously and regularly.

- 11) Aspirin, Dimenhydrinate and Caffeine shows faster absorption through MCG than tablets,
- 12) Stimulates flow of saliva in the mouth,
- 13) Neutralizes plaque acids that form in the mouth after eating fermentable carbohydrates,
- 14) Helps whiten teeth by reducing and preventing stains.

Demerits of Medicated Chewing Gum

- 1) 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,
- 2) Sorbitol present in MCG formulation may cause flatulence, diarrhea,
- 3) Additives in gum like flavoring agent, Cinnamon can cause Ulcers in oral cavity and Liquorice cause Hypertension,
- 4) Chlorhexidine oro-mucosal application is limited to short term use because of its unpleasant taste and staining properties to teeth and tongue,
- 5) Chewing gum have been shown to adhere to different degrees to enamel dentures and fillers,
- 6) Prolong chewing on gum may result in pain in facial muscles and earache in children.

Composition of Medicated Chewing Gum

1. Gum Base

Gum base is an inert and insoluble nonnutritive product used as a support for the edible and soluble of the chewing gum (sugar, glucose, poly oils and flavors) other raw materials are generally grouped in the following classes.

2. Elastomers

Including natural and synthetic rubbers. The gum base composition may contain conventional elastomer solvents to aid in softening the elastomer base component. Such elastomer solvents may comprise terpinene resins such as polymers of alpha-pinene or beta-pinene, methyl, glycerol or pentaerythritol esters of resins or modified resins and gums, such as hydrogenated, dimerized or polymerized resins or mixtures. The elastomer solvents may be employed in amounts from 5.0% to 75.0%, by weight of the gum base, and preferably from 45.0% to 70.0%, by weight of the gum base.

Synthetic elastomers such as butadiene, styrene copolymers, polyisobutylene, isobutylene isoprene copolymers, polyethylene mixtures, and non-toxic vinyl polymer, such as polyvinyl alcohol are widely used bases. The molecular weight of the vinyl polymer may range from 3,000 to 94,000. The amount of gum base employed varies greatly depending upon various factors such as the type of base used, the consistency of the gum desired and the other components used in the composition to make the final chewing gum product. In general, the gum base will be present in amount from 5% to 94%, by weight of the final chewing gum composition. Preferably, the gum base is used in amounts from 15% to 45% and more preferably in amounts from 15% to 35% by weight of the final chewing gum composition.

3. Plasticizers

Waxes, vegetable oils, glycerides. Plasticizers or softeners such as lanolin, palmitic acid, oleic acid, stearic acid, sodium stearate, potassiumstearate, glyceryl triacetate, glyceryl lecithin, glycerylmonostearate, propylene glycol monostearate, acetylated monoglyceride, glycerine, natural and synthetic waxes, hydrogenated vegetable oils, polyurethane waxes, paraffin waxes, microcrystalline waxes, fatty waxes, sorbitolmonostearate, propylene glycol, may be incorporated into the gum base to obtain a variety of desirable textures and consistency properties.

4. Adjuvants

Calcium carbonate, talc, or other charging agents are used. Mineral adjuvant such as calcium carbonate, magnesium carbonate, aluminum hydroxide, aluminum silicate, talc, tricalcium phosphate, dicalcium phosphate serve as fillers and textural agents.

5. Antioxidants

An anti-oxidant such as butylated hydroxytoluene, butylated hydroxyanisole, propyl gallate and mixtures thereof, may be included as antioxidants.

6. Compression adjutants

Suitable compression adjuvant such as silicon dioxide, magnesium stearate, calcium stearate and talc can be used in medicated chewing gum for ease of compression. The alkaline earth metal phosphates and alkali metal phosphates prevent caking and balling of

“High” i.e. 2 to 8% moisture-containing chewing gum compositions during grinding. Additionally, it has been discovered that maltodextrin enhances the grinding of “high” moisture-containing chewing gum compositions by absorbing moisture to allow lubrication in the gum as it separates into granules. If oil lubricants are used, it is preferred to be 0.4% to 1% by weight of the tableted chewing gum composition. The amount of glidant present in the tableted chewing gum composition is from 0.5% to 5% by weight of the tableted chewing gum composition. Those glidants useful are selected from the group consisting of alkali metal salts, talc, starch, polyhydric alcohols and mixtures. Antiadherents function to prevent tablet granulations from sticking to the faces of the punches and the die walls, but most importantly, prevent adherence of chewing gum granules from adhering to one another, a phenomenon known as blocking. Anti-adherents may be added to the chewing gum composition while the composition is in the hoppers, or subsequent to grinding and are selected from the group consisting of silicates, silicon dioxide, talc and mixtures thereof present in amount of 0.2% to 1% by weight of the tableted chewing gum composition and preferably about 0.3 to about 0.6% by weight. Generally anti-adherent is a finely divided low bulk density powder, which is preferably water insoluble. The preferred antiadherents are fumed silica and talc. The term-fumed silica is meant to include pyrogenic silicas, micron sized silicas and hydrated silicas.

7. Sweeteners

a) Water-soluble sweetening agents

Xylose, ribulose, glucose, mannose, galactose, fructose, sucrose, maltose, invert sugar partially hydrolyzed starch, dihydrochalcones, monellin, steviosides, glycyrrhizin, and sugar alcohols such as sorbitol, mannitol, hydrogenated starch hydrolysates.

b) Water-soluble artificial sweeteners

Soluble saccharin salts, i.e. sodium or calcium saccharin salts, cyclamate salts.

c) Dipeptide based sweeteners

L Aspartic acid derived sweeteners such as Aspartame, Alitame, methyl esters of L-

aspartyl-L-phenylglycerine and L-aspartyl-L-2,5-dihydrophenylglycine, L-aspartyl 2,5-dihydro-L-phenylalanine – L aspartyl – L (1-cyclohexen) alanine.

d) Water-soluble sweeteners

Derived from naturally occurring water soluble sweeteners, chlorinated derivatives of ordinary sugar (sucrose, known as Sucralose)

e) Protein based sweeteners

Such as thaumaococcus danielli (Thaumatococcus I and II) In general an effective amount of sweetener is utilized to provide the level of sweetness desired, and this amount will vary with the sweetener selected and are present in amounts from 0.0025% to 90% by weight of the gum composition.

8. Coloring Agents

The coloring agents include pigments, which may be incorporated in amounts up to about 6% by weight of the gum composition, titanium dioxide may be incorporated in amounts up to about 2%. The colorants may also include natural food colors and dyes suitable for food drug and cosmetic applications.

9. Flavoring Agents

Flavoring agents suitable for use are essential oils and synthetic flavors such as citrus oils, fruit essences, peppermint oil, spearmint oil, clove oil wintergreen oil, and anise oil.

Table 1: Optimal Properties of Drug.

	High Salivary Solubility
Physicochemical Properties of Drug	pH independent solubility
	Tasteless
	Non-toxic to oromucosa and salivary ducts
	Non-carcinogenic
Patient Related Factors	Should not cause tooth decay
	Should not cause oromucosa and teeth staining
	Should not affect salivary flow rate

10. Active Component

In medicated chewing gum active pharmacological agent may be present in core or coat or in both. The proportion of which may vary from 0.5-30% of final gum weight. A small, unionized, lipophilic and enzymatically stable active agent is likely to be absorbed more readily. A saliva soluble ingredient will be completely released within 10-15 minutes of chewing whereas lipid soluble ingredient will dissolve in the gum base and thereafter be slowly and completely absorbed. MCG consists of masticatory gum core that may be coated. The core is composed of an aqueous insoluble gum base which can be mixed with Sweeteners and Flavours. The coating can be applied as a film of polymers, waxes, sweeteners, flavours and colours or a thick layer of sugar or sugar alcohol.

Manufacturing Processes

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

1. Conventional/Traditional method (Fusion)

Components of gum base are softened or melted and placed in a kettle mixer to which sweeteners, syrups, active ingredients and other excipients are added at a definite time. The gum is then sent through a series of rollers that forms 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.

Limitations

1. Elevated temperature used in melting restricts the use of this method for thermoliable drugs.
2. Melting and mixing of highly viscous gum mass makes controlling of accuracy and uniformity of drug dose difficult.
3. Lack of precise form, shape or weight of dosage form.
4. Technology not so easily adaptable to incorporate the stringent manufacturing

conditions required for production of pharmaceutical products.

5. Such a chewing gum composition is difficult to form into chewing gum tablets because of their moisture content (2-8%). If attempted to grind and tablet such a composition would jam the grinding machine, stick to blades, screens adhere to punches and would be difficult to compress.

2. Cooling, Grinding and Tableting Method (Thermoliable)

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

Cooling and Grinding

The CG 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 CG 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. Amongst the various coolants like liquid nitrogen, hydrocarbon slush use of solid carbon dioxide is preferred as it can give temperatures as low as -78.5 °C, it sublimates readily on warming the mixture, is not absorbed by the chewing gum composition, does not interact adversely with the processing apparatus and does not leave behind any residue which may be undesirable or potentially hazardous. The refrigerated composition is then crushed or ground to obtain minute fragments of finely ground pieces of the composition. Alternatively, the steps of cooling the chewing gum composition can be combined into a single step. As an example, cooling the grinding apparatus itself which can be done by contacting the grinding apparatus with a coolant or by placing the grinding apparatus in a cooling jacket of liquid nitrogen or other cold liquid. For more efficient cooling, the chewing gum composition can be pre cooled prior to cooling to the refrigeration temperature. Sometimes a mixture of chewing gum composition, solid carbon dioxide and

precipitated silica is ground in a mill grinder in the first step. Additional solid carbon dioxide and silica are added to the ground composition, and the composition is further ground in the second step. This two step grinding process advantageously keeps the chewing gum composition at a very low temperature. The presence of solid carbon dioxide also serves to enhance the efficiency of the grinding process. The same process can be made multiple by adding incorporating additional carbon dioxide and/or precipitated silica at each step. Certain additives can be added to the chewing gum composition to facilitate cooling, grinding and to achieve desired properties of chewing gum. These include use of anti-caking agent and grinding agent.

Use of anti-caking agent

An anti-caking agent such as precipitated silicon dioxide can be mixed with chewing gum composition and solid carbon dioxide prior to grinding. This helps to prevent agglomeration of the subsequently ground chewing gum particles.

Use of grinding agents

To prevent the gum from sticking to the grinding apparatus, 2-8% by weight of grinding aid such as alkaline metal phosphate, an alkaline earth metal phosphate or maltodextrin can be incorporated. However practical use of these substances is limited because these substances are highly alkaline and hence would be incompatible with acidic ionisable therapeutic agents. They also tend to remain in the composition and final chewing gum tablet and thus may be problematic for therapeutic and safety point of view.

Tabletting

Once the coolant has been removed from the powder, the powder can be mixed with other ingredients such as binders, lubricants, coating agents, sweeteners etc, all of which are compatible with the components of the chewing gum base in a suitable blender such as sigma mill or a high shear mixer. Alternatively a Fluidized Bed Reactor (FBR) can be used. The use of FBR is advantageous as it partially rebuilds the powder into granules, as well as coats the powder particles or granules with a coating agent thereby minimizing undesirable particle agglomeration.

The granules so obtained can be mixed with antiadherents like talc. The mixture can be blended in a V type blender, screened and staged for compression. Compression can be carried out by any conventional process like punching. It requires equipment other than conventional tableting equipment and requires careful monitoring of humidity during the tableting process which is the major limitation.

3. 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. "Generally regarded as safe" (GRAS). Pharmagum® is available in three forms namely S, M and C. Pharmagum® M has 50% greater gum base compared to Pharmagum®S. Pharmagum®S consists primarily of gumbase and sorbitol. Pharmagum®M contains gumbase, mannitol & Isomalt. Releases of nicotine from directly compressible nicotine gum formulations and from Nicorette® prepared by conventional methods have shown that use of Pharmagum in formulation showed a faster release rate. Formulations made with Pharmagum® M & S are similar to tablet in appearance. Gums formed using compressible formulation are 10 times harder and crumble when pressure is applied resulting in faster release than conventional methods. Use of Pharmagum S, M and C enables formulators to utilize a gum delivery system quickly & more cost effectively than by traditional methods.

Factors Affecting Release of Active Ingredient

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

2. Physicochemical properties of active ingredient: It plays a 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.

3. 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.

4. 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.

Some Important Formulation Aspect

- 1) Increased amount of softeners and emulsifiers in gum base fasten release whereas hard gum may retard,
- 2) Cyclodextrin complexation or solubilisation technique increases aqueous solubility of drugs that are poorly water soluble,
- 3) A solid system of lipophilic active ingredients bound to the cation exchange resin permits a sustained drug delivery system,
- 4) Microencapsulation or agglomerations are the methods to modify and control the release of active ingredient.

Table 2: Some of the commercially available chewing gum and trade mark.

Sl. No.	Trade Mark(™)	Active substance	Aim	Commercial availability
1	Aspergum	Aspirin	Pain Relief	North America
2	Nicorette	Nicotine	Smoking cessation	World wide
3	Nicotinelle	Nicotine	Smoking cessation	Western Europe, Australia, New Zealand
4	Travell	Dimenhydrinate	Travel illness	Italy, Switzerland
5	Go Gum	Guarana	Alertness	Australia
6	Chooz	Calciumcarbonate	Stomach acid , neutralization	USA
7	Endekay Vit C	Vit C	General health	Middle east United Kingdom
8	Brain	DHA and CCE	Enhanced brain activity	Japan
9	Stay alert	Caffeine	Alertness	USA
10	Stamil Vit C	Vit C	General health	Australia
11	Café Coffee	Caffeine	Alertness	Japan
12	Buzz Gum	Guarana	Alertness	United Kingdom
13	Chroma slim	CR	Diet	USA

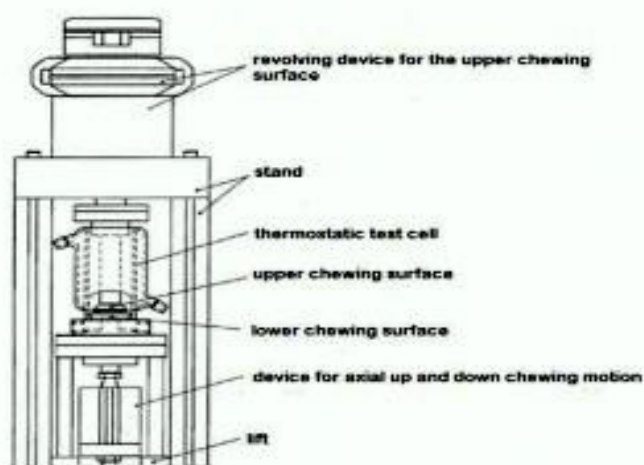


Fig. 1: schematic representation of unofficial single module chewing apparatus.

In-Vitro Drug Release Testing Apparatus

Number of apparatus for studying in-vitro drug release from medicated chewing gum has been developed. An apparatus for in vitro drug release testing of medicated chewing gums has been developed and studied for the effect of chewing surfaces, twisting movements of surfaces and temperature of test medium on release rate of drug from MCG by Kvist C et al. Another novel dissolution apparatus has been developed for MCG by Rider JN et al. The apparatus consist of conical teflon base and a rotating, ribbed teflon plunger suspended in a dissolution vessel. The rotation speed, plunger frequency, medium volume, medium type, medium sampling location, number of plunger ribs and number of gum pieces were studied. In 2000, European Pharmacopoeia published a monograph describing a suitable apparatus for studying the in-vitro release of drug substances from MCG. The chewing machine consists of a temperature-controlled chewing chamber in which the gum piece is chewed by two electronically-controlled horizontal pistons driven by compressed air. The two pistons transmit twisting and pressing forces to the gum, while a third vertical piston, ("tongue") operates alternately to the two horizontal pistons to ensure that the gum stays in the appropriate position. The temperature of the chamber can be maintained at $37\pm 0.5^{\circ}\text{C}$ and the chew rate can be varied. Other adjustable settings include the volume of the medium, the distance between the jaws and the twisting movement. The European Pharmacopoeia recommends 20 ml of unspecified buffer (with a pH close to 6) in a chewing chamber of 40 ml and a chew rate of 60 strokes per minute. Single module chewing apparatus is shown in the fig. 1.

Factors affecting release of active ingredient from MCG

Person-to-person variability: One of the reasons why MCG has not yet been fully exploited is because of the therapeutic uncertainty related to the drug delivery method that is, a patient's mechanical chewing action. The gum's therapeutic effect depends on chewing and as each person has his/her own

chewing force, frequency and chewing time, which may lead to variation in results. The rate at which the subject chews gum also affects the amount of drug released. The average chewing rate is ~ 60 chews every minute. For this purpose, the release of nicotine from Nicorette chewed at different rates has been investigated. In that study it was found that a chewing rate of 1 chew every second gave a significantly ($p < 0.05$) higher release than a chewing rate of 1 chew every 8 s. An in vitro study prescribed by European Pharmacopoeia suggests 60 strokes a minute are sufficient for proper release of active ingredient.

Physicochemical properties of drug: The physicochemical properties of the active ingredient such as its molecular mass, ionized or non-ionized form, lipophilicity or hydrophilicity, stability to salivary enzymes (amylase) and its solubility in salivary fluid play very important roles in the release of drug from MCG and absorption of drug through oral mucosa. For example, the saliva-soluble ingredients will be immediately released within a few minutes, whereas lipid-soluble drugs are released first into the gum base and then slowly into salivary fluid. Aqueous solubility of API plays an important role in the release from chewing gum composition, that is, release of water-soluble drug (aqueous solubility $> 1:10$) is, in general, ~ 75% or more during 5 min of chewing and 90% or more during 15 min of chewing at a rate of 60 chews a minute. Drugs with aqueous solubility between 1:10 and 1:300 demonstrate up to 60% release during 10 min of chewing and between 50 and 90% release after 15 min of chewing.

Formulation factors: Composition and amount and type of gum base, solubilizing agents and softening agents may affect the rate of release of the active ingredient from MCG.

Possible absorption pathways: The release of most water-soluble components from chewing gum is relatively rapid. Drug released from the chewing of medicated gum will be either absorbed from the buccal mucosa or, if swallowed, absorbed from the gastrointestinal tract. Drugs that are released from chewing gum and involuntarily swallowed will be introduced to the gastrointestinal tract in

dissolved, diluted, or suspended form in saliva and so will be very easily bioavailable with a consequent fast onset of action as compared with solid oral dosage forms. To obtain the optimal formulation it is possible to decrease the release rate of highly hydrophilic substances and increase the release rate of lipophilic substances. Antihistamines (chlorpheniramine maleate, cetirizine HCl), appetite suppressants (phenylpropanolamine HCl or caffeine), expectorants (guifensin hydrochloride), antitussives (dextromethorphan, noscapine), opioids (codeine phosphate, codeine sulfate), nasal decongestants (phenylephrine HCl, pseudoephedrine, ephedrine HCl), analgesics and anti-pyretics (aspirin or acetaminophen), anti-inflammatories (ibuprofen, ketoprofen, naproxen), electrolyte and mineral supplements, antacids, laxatives, vitamins, ion exchange resins (cholestyramine), and anti-cholesteralamics such as most prescribed therapeutic categories can be potential possible targets for delivery in the form of MCG owing to its higher patient compliance and quick onset of action.

Stability

The stability of chewing gum is comparable to that of most other solid delivery systems. Chewing gum normally contains little water (2.5%). If the water content is very critical for the stability of drug, the chewing gum can be manufactured without water (less 0.2%). This will however, often make the product hygroscopic and will affect the texture. The low water content also inhibits microbial growth in the chewing gum during storage. Furthermore, the product can be protected against oxidation by a sealed coat and by an appropriate packing. For every temperature-labile component, e.g. enzymes, the process temperature of 50-600°C during mixing may create a stability problem. It is however possible to operate the process at a lower temperature to avoid this issue.

Applications

1. Dental caries

- a. Prevention and cure of oral disease are targets for chewing gum formulations.
- b. It can control the release rate of active substances providing a prolonged local effect.

c. It also re-elevates plaque pH which lowers intensity and frequency of dental caries.

d. Fluoride containing gums have been useful in preventing dental caries in children and in adults with xerostomia.

e. Chlorhexidine chewing gum can be used to treat gingivitis, periodontitis, oral and pharyngeal infections.

f. It can also be used for inhibition of plaque growth.

g. Chlorhexidine chewing gum offers numerous flexibility in its formulation as it gives less staining of the teeth and is distributed evenly in the oral cavity.

h. The bitter taste of chlorhexidine can be masked quite well in a chewing gum formulation.

2. Systemic therapy

a) Pain-

Chewing gum can be used in treatment of minor pains, headache and muscular aches.

b) Smoking cessation-

Chewing gum formulation containing nicotine and lobeline have been clinically tested as aids to smoking cessation.

c) Obesity-

Active substances like chromium, guaran and caffeine are proved to be efficient intreating obesity. Chromium is claimed to reduce craving for food due to an improved blood-glucose balance. Caffeine and guaran stimulate lipolysis and have a thermogenic effect (increased energy expenditure) and reduce feeling of hunger.

d) Other indications-

Xerostomia, Allergy, Motion sickness, Acidity, Cold and Cough, Diabetes, Anxiety, etc are all indications for which chewing gum as drug delivery system could be beneficial.

Future Opportunities

Chewing gum not only offers clinical benefits but also is an attractive, discrete and efficient drug delivery system. Nowadays more and more disease can be treated with Novel Drug Delivery Systems. Generally, it takes time for a new drug delivery system to establish itself in the market and gain acceptance and popularity by the patients, however chewing gum is believed to manifest its position as a convenient and advantageous drug delivery system as it meets the high quality standards of pharmaceutical industry and can be

formulated to obtain different release profiles of active substances. Finally, in the future, we may see that more and more drugs formulated into chewing gum in preference to other delivery systems to deliver drugs locally to the oral cavity. The reason is simple that the chewing gum delivery system is convenient, easy to administer anywhere, anytime and its pleasant taste increases the product acceptability and patient compliance.

Conclusion

Chewing gum is an excellent drug delivery system for self-medication, as it is convenient and can be administered discretely without water. It offers several advantages compared to chewable tablets, lozenges and other related formulations. Hence in forth coming years it will become a much more common and popular drug delivery system. The potential of MCG for buccal delivery, fast onset of action and the opportunity for product-line extension makes it an attractive delivery form. Reformulation of an existing product is required for patent protection, additional patient benefits and conservation of revenues.

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Source of Support: Nil. Conflict of Interest: None declared
