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MEDICATED CHEWING GUM-A NOVEL DRUG DELIVERY TECHNIQUE FOR SYSTEMIC AND TARGETED DRUG DELIVERY

K.Ezhumalai*, P. Ilavarasan, A.N.Rajalakshmi, U. Sathiyaraj, R. Murali Mugundhan

Mother Theresa Post Graduate and Research Institute of Health Sciences, Puducherry–605 006

Email: ezhumalai.811@gmail.com

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ABSTRACT

Chewing gums are mobile drug delivery systems. The world market for chewing gum is estimated to be 560,000 tons per year, representing approximately US $5 billion. Some 374 billion pieces of chewing gum are sold worldwide every year, representing 187 billion hours of gum-chewing if each piece of gum is chewed for 30 minutes. Medicated Chewing Gum (MCG) is a novel drug delivery system containing masticatory gum base with pharmacologically active ingredient and intended to use for local treatment of mouth diseases or systemic absorption through oral mucosa. The introduction and subsequent success of nicotine chewing gum in the 1980s paved the way for a more general acceptance of chewing gum as a drug delivery system. Unlike chewable tablets medicated gums are not supposed to be swallowed and may be removed from the site of application without resort to invasive means and MCGs are solid, single dose preparations. As for as patient convenience is concerned it is discrete and easy administration without water promotes higher compliance. Since it can be taken anywhere, a chewing gum formulation is an excellent choice for acute medication. The advantages for children and for patients who find swallowing tablets difficult are obvious.This review mainly tells about history,compostion of MCG, in-vitro drug release testing apparatus and future trends.

KEYWORDS: Chewing gums, mobile drug delivery system, dental caries, mouth diseases, saliva.

INTRODUCTION

It is well known fact that the right drug delivery system is critical to the success of a pharmaceutical product. 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. In addition to its confectionary role, Chewing Gum (CG) also has proven value as a delivery vehicle for pharmaceutical and nutraceutical ingredients[(1)].

A novel drug delivery system creates additional patient benefits that will add new competitive advantages for a drug and thus increase revenue. Oral route is the most preferred route amongst the patient and clinicians due to various advantages it offers. One of the reasons that the oral route achieved such popularity may be in part attributed to its ease of administration[(2)]. Many scientific studies have explored the role of chewing gum in promoting healthy teeth. Gum chewing is a common habit in many countries. Although gum chewing offers great pleasure to many individuals, it is also a nemesis for countless parents, school teachers and building custodians because this sticky intruder is often found in children's hair, on bed posts, and under tables, chairs, desks or sticks to the soles of passing shoes[(3)]. Chewing gum has been used for centuries to clean the mouth and freshen the breath[(4)]. The first patent for the production of chewing gum was filed in 1869 and was issued to Mr. W. F. Semple in Ohio under U. S. Patent No. 98,304. A MCG containing Acetyl Salicylic Acid was commercially introduced in 1928[(5)]. In 1991, Chewing Gum was approved as a term for pharmaceutical dosage form by the commission of European Council. Approximately £80 to 100 million, 55% of it being sugar free gum. Seventy-nine percent of the chewing gums sold in Switzerland are sugar-free, 70% of the consumers are teenagers, and girls chew more gum than boys.

There is no doubt that chewing gum is an important factor in confectionery and that it can be expected to have an influence on dental health [(6)]. Chewing gum was initially sweetened with sugar, which contributed to dental caries. Today, however, more than 50% of chewing gum sold in Europe is sweetened with sugar substitutes (polyols). Clinical evidence shows that sugar substituted chewing gum does not lead to caries, because the polyols do not lead to a clinically relevant production of metabolic acids in dental plaque. At the same time, however, gum-

chewing stimulates the flow of saliva, thus strengthening its protective properties, i.e., its buffering capacity, mineral supersaturating, and cleansing, antimicrobial, and agglutinating actions. Clearly, this suggests a beneficial effect from the chewing of sugar-free gum[7] .

The science is supported by expert reviews and statements from authoritative bodies indicating that chewing sugar free gum can help reduce the risk of dental caries (cavities). The objective of this systematic literature review was to appraise existing evidence concerning a possible therapeutic / anti-carcinogenic effect of sugar-free chewing gum for patients. MCG represents the newest system with potential uses in pharmaceuticals, over the counter medicines and neutraceuticals[8]. The drugs intended to act in oral cavity often have low water/saliva solubility and chewing gum constitute a valuable delivery system for such drugs.

Chewing gum is used widely. A devoted gum chewer can confidently transverse the globe with the assurance that his/her masticatory needs will be met. These are some of the international terms which identify chewing gum (e.g. goma de mascara in Argentina; kaugummi in Austria; le chewing gum in France; ellk in Arabian area; tskles in Greece; gamu in Japan, tyggegummi in Norway and heung how chu in Taiwan). So it can be considered as an international habit among all countries of the world (except in some countries and in some religious communities where gum chewing is still considered as bad manners or even forbidden e.g. Singapore & UAE).

The production and distribution of chewing gum is a multimillion dollar business which continues to expand. In 1987, gum products accounted for 550 million dollars in sales in the USA.Chewing gum provides new competitive advantages over conventional drug delivery system.

HISTORY[9]

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 MAINEPURE 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.l. 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 sorbital 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 MCG[1,5]

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. Duration of action is increased,
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 MCGS[4,10,11,12,13]

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.

Chewing Gum and Saliva[14]

Chewing gum stimulates one of the most powerful defense mechanisms in the body – saliva. Saliva is vital to good oral health.

Saliva has three main protective (anti-caries) functions: (1) dilutes and washes away food debris; (2) the bicarbonate neutralizes and buffers plaque acids; and (3) the calcium and phosphate ions contribute to remineralization of early dental caries lesions. Saliva also contains antibacterial agents.

Saliva alone is a powerful protector of the oral cavity. And, chewing gum is an efficient and pleasant way to increase saliva without drugs. Increasing saliva in the mouth is accomplished by the stimulation of flavors and the gustatory action of chewing.

Together these forces stimulate the salivary glands to increase their flow rate by about 10 times the resting state during the first few minutes of chewing and keep it significantly elevated for as long as one chews.

Taste and Texture[15]

To succeed in the market, the chewing gum formulation must have a pleasant taste and texture. Most active substances have an unpleasant, bitter or metallic taste. Since the active substance will be released in the oral cavity and remain there for a longer period of time than in the case with ordinary delivery forms (usual chewing time is 10 to 20 minutes), unique expertise in taste definition, taste masking and taste modification are essential for the success of a medical chewing gum product. Moreover, there are no official standards for unpleasant taste, making it necessary to establish information on taste properties for all new active substances. In most cases, it is desirable that the taste fades out when the active substance has been fully released. The release profile of the flavours and sweeteners, therefore, is usually designed to follow the release profile of the active substance.

One of the major challenges for the product developer is that any small adjustment in the amount of active substances, flavours and sweeteners often changes the gum base texture, requiring adjustments to tailor-make the gum base to the active substance. During the development process, therefore, it is necessary to test several parameters related to taste and texture continously.

COMPOSITION OF MCGS[16]

Chewing gum 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 CG is natural gum Chicle, obtained from the sapodilla tree. Chicle is very expensive and difficult to procure therefore other natural gum or synthetic materials like polyvinylacetate and similar polymers can be used as gum base.

Typically Chewing Gum comprises two parts viz,

1. Water insoluble gum base generally comprises Elastomers, Resins, Fats and Oils, and Inorganic fillers

a) Elstomers: Elastomer provides elasticity and controls gummy texture. Natural elastomer which is a natural rubber like Latex or Natural gum such as Jelutong, Lechi Caspi, Perillo, Chicle.

b) Plastisizers: Which are used to regulate cohesiveness of product and are divided into Natural and Synthetic.

- Natural Plastisizers - Natural resin esters like Glycerol esters or partially hydrogenated resin, Polymerized glycerol esters, Glycerol esters of partially dimerized resin & Pentaerythritol esters of resin.
- Synthetic Plastisizers - Terpene resins derived from α-pinene and/or d-limonene.

c) Fillers or Texturizers*:* Provide texture, improve chewability, provide reasonable size of the gum lump 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/ Ttri Calcium Phosphate.

2. Water soluble portions contain Bulk Sweetners, High intensity Sweetners, Flavouring agents, Softners, Emulsifiers, Colours and Antioxidants

a) Softners and Emulsifiers: These are added to the chewing gum in order to optimize the chew ability and mouth feel of the gum. Softners include Glycerin, Lecithin, Tallow, Hydrogenated Tallow, Mono/ Di/ Tri-Glycerides, Fatty acids like Stearic acid, Palmitic acid, Oleic acid and Linoleic acid.

b) Colourants and Whiteners may include FD & C type dyes and lakes, fruit and vegetable extracts, Titanium Dioxide.

c) Sweetners: These are of two types, Aqueous and Bulk.

- Aqueous Sweetners can be used as softners to blend the ingredients and retain moisture. These include Sorbitol, Hydrogenated Starch Hydrolysates and Corn Syrups. Corn syrup keeps gum fresh and flexible.
- Bulk Sweetners include Sugar and Sugarless components. Sugar components include Saccharides like Sucrose, Dextrose, Maltose, Dextrin, Fructose, Galactose and Corn Syrup. Sugarless components include sugar alcohols such as Sorbitol, Manitol, Xylitol, Hydrogenated Starch Hydrolysate. High intensity artificial sweetners can also be included to provide longer lasting sweetness and flavour perception e.g. Sucralose, Aspartame, salt of Acesulfame, Alitame, Saccharin, Glycerrhizin, Dihydrochalcones.

d) Bulking agents: These are used if low calorie gum is desired. Examples of low calorie bulking agents include Polydextrose, Oligofructose, Inulin, Guargum hydrolysate, Indigestible Dextrin.

e) Flavouring Agents: A variety of flavouring agents are used to improve flavour in chewing gum includes essential oils, such as Citrus oil, fruit essences, Peppermint oil, Spearmint oil, Mint oil, Clove oil & Oil of Wintergreen. Artificial flavouring agents can also be used.

f) 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 Sweetners and Flavours. The coating can be applied as a film of polymers, waxes, sweetners, flavours and colours or a thick layer of sugar or sugar alcohol. The optimal properties of active ingredient in MCG are shown in Table 1.

Table 1: Optimal Properties of Drug.

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

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 sweetners, syrups, active ingredients and other excipients are added at a definte 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[17]

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 Tabletting 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[18]

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^{o}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^{o}C, it sublimes 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 & staged for compression. Compression can be carried out by any conventional process like punching. It requires equipment other than conventional tabletting equipment and requires careful monitoring of humidity during the tabletting process which is the major limitation.

3. Use of direct compression chewing gum excipients[19]

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 a mixture of polyol(s) and/or sugars with a chewing gum base. It is available as directly compressible powder, free flowing powder which can be compacted into a gum tablet using conventional tablet press thus enabling rapid and low cost development of a gum delivery system. It is manufactured under CGMP conditions and complies with Food Chemicals Codex specifications as well as with FDA, so they can be considered as "Generally regarded as safe" (GRAS).

FACTORS AFFECTING RELEASE OF ACTIVE INGREDIENT[20]

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[21,22]

1) Increased amount of softners 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 agglomeration are the methods to modify and control the release of active ingredient.

SOME OF THE COMMERCIALLY AVAILABLE CHEWING GUM AND TRADE MARK.

SI. 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	Superpep	Dimenhydrinate	Travel illness	Germany, Switzerland

6	Chooz	Calciumcarbonate	Stomach acid , neutralization	USA
7	Endekay Vit C	Vit C	General health	Middle east United Kingdom
8	Stamil Vit C	Vit C	General health	Australia
9	Brain	DHA and CCE	Enhanced brain activity	Japan
10	Stay alert	Caffeine	Alertness	USA
11	Café Coffee	Caffeine	Alertness	Japan
12	Buzz Gum	Guarana	Alertness	United Kingdom
13	Go Gum	Guarana	Alertness	Australia
14	Chroma slim	CR	Diet	USA

IN-VITRO DRUG RELEASE TESTING APPARATUS[23,24]

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±0.5°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 figure1.

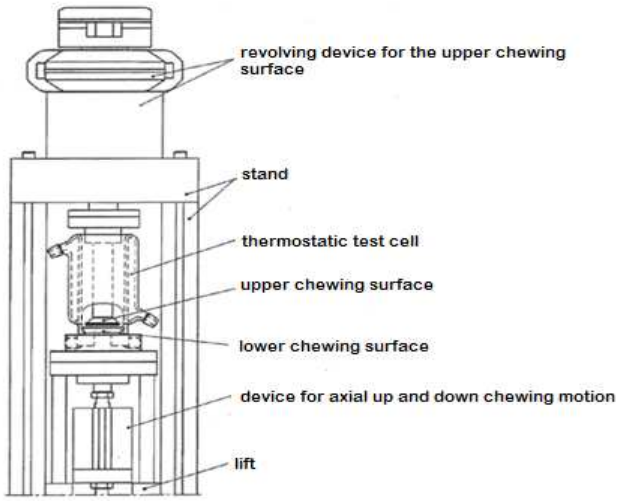

Figure 1: Single module chewing apparatus from Wennergren

Applications[25,26,27]:

1. Dental caries:

a. To prevent and cure oral disease is the main target of MCG formulations.

b. To control the release rate of active substances and to provide a prolonged local effect.

c. To re-elevate plaque pH which lowers intensity and frequency of dental caries.

d. Fluoride containing gums have been used to prevent 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. To inhibit plaque growth.

g. Chlorhexidine chewing gum offers numerous flexibility in its formulation for less staining of the teeth and for even distribution in the oral cavity.

h. To mask the bitter taste of chlorhexidine.

2. Systemic therapy:

a) Pain- 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 in treating 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.

LIMITATIONS OF CHEWING GUM AS DRUG DELIVERY SYSTEM [28]

Chewing gum has several disadvantages as the drug released into saliva disappears rapidly from the oral cavity because of involuntary swallowing. The concentration of drug in the oral cavity always tends to decrease as a result of salivary dilution. Drug release from chewable formulations has shown to be strongly influenced by the way patient chews the formulation. Administration of such dosage form is restricted to short period of time because the presence of the delivery system in the oral cavity causes disturbance in drinking, eating and speaking. Despite

these limitations, chewing gum formulation affords extended delivery period compared to solution and fast dissolving tablets.

SAFETY ASPECTS

Difference commercial chewing gums have been shown to adhere to different degree to dentures, fillers and crowns. Over chewing causes painful jaw muscles. Chewing gum appears to offer a smaller risk of overdosing by mistake or misuse than flavored chewable tablets. Medicated chewing gums should, like other medicaments, be kept out of reach of children and it would be wise to advice people prone to allergic responses to check the flavoring and sweetening agents included in the chewing gum formulations.

FUTURE TRENDS

Chewing gum not only offers clinical benefits but also is an attractive, discrete and efficient drug delivery system. A few decades ago, the only treatment for some disease was surgical procedure but now more and more diseases 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 by 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. Clinical trials and market research have proven this to be the case. In the coming years it is very likely that new formulations will enter the market and that chewing gum will become a common drug delivery system.

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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Corresponding Author:

K.Ezhumalai*,

Mother Theresa Post Graduate and Research Institute of Health Sciences,

Puducherry – 605 006.

Email: *ezhumalai.811@gmail.com*