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MEDICATED CHEWING GUM: WONDER THERAPY

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ABSTRACT
Medicated chewing gum are the novel oral drug delivery system which can be use for both local and systemic action. MCG are the solid single dose preparation which are intended to be chew and they are not supposed to be swallowed thus this type of drug delivery system provide prompt termination of therapy at anytime which provide a very distinct advantage over other oral novel drug delivery system. MCG provide high degree of patient compliance as it is easy for administration without water it is found. Now a days medicated chewing gum therapy are more seen as the prophylaxis therapy and there is large market of medicated chewing gum which are used for oral health like fluorides containing chewing gum for dental caries, aspirin containing for analgesic etc. Medicated chewing gums contain a gum base which is a heart of the preparation which provide the chewing gum its chewing consistency and other desired properties like strength, texture, surface, plasticity. apart from gum base it contain other supporting ingredients which enhances the look and appearance of chewing gum and make it market ready like flavourant, colourant, sweetener. the present review article will enlighten everyone with nicely discussed advantages and disadvantages, composition, manufacturing method, factor affecting release of active ingredients, evaluation and quality control parameter, application, future trend of medicated chewing gum.

KEYWORDS: Chewing gum, Prophylaxis therapy, Dental caries, Gum base.

INTRODUCTION[1-9]
Chewing gum a novel oral drug delivery system which can be used both locally as well as systematically. scientist and researcher have done several enhancement in terms of technological and scientific aspect of chewing gum so it can be developed into safe and efficacious preparation which can be effectively used. Medicated chewing gum contain unique ingredient which is called gum base which provide masticatory property. MCG is considered as a medium of drug delivery to administer pharmacological active ingredient that can improve health and nutrition. Earlier the use of chewing gum is to provide some nutrition benefits or where used as a mouth freshner it is the development which led to use chewing gum for the purpose of treatment of some diseases. For drug which intended to act in oral cavity but often have low water/saliva solubility in this scenario chewing gum preparation helps to overcome this problem. MCG is solid or semi solid preparation in which active ingredient which is either water soluble or water insoluble is dispersed in water insoluble gum base.

Many scientific studies shown that gum chewing is normal habit in many countries chewing gum was traditionally used for cleaning the teeth, mouth and to freshen the breathe. A MCG containing acetyl sailicylic acid was manufactured in 1928. In 1991 European council approved the chewing gum as official pharmaceutical dosage form. It was observed that that the gum release drug at a desired rate and it can be compared with the modified release dosage form. These drug delivery system permits more therapeutic action compared to per-oral dosage forms. Drugs that have been incorporated till now are mouth freshner, anti emetic, metabolism enhancers, motion sickness, most of which use for smoking cessation or for the oral hygiene. Historically chewing gum was an important factor in confectionery. Chewing gum was initially sweetened with sugar which led to dental caries further development led to replacement of sugar with substituted with polyols as sweetened agent in Europe today 50% of the chewing gum are prepared using polyols. It is found that polyols doesn't cause the dental carries because polyols do not lead to formation of metabolic acid which lead to dental plaquen 1987, gum products accounted for 550 million dollars in sales in the USA. Chewing gum provides new competitive advantages over conventional drug delivery system. Several ingredients are now incorporated in medicated chewing gum, e.g. fluoride for prophylaxis of dental caries, chlorhexidine as local disinfectant, nicotine for smoking cessation, aspirin as an

analgesic, and caffeine as a stay alert preparation. US market accounts for approx. 50% of world market for medicated chewing gums.

The mechanism is such that during chewing the drug contained in the gum is released into saliva the drug which got released is either get 1 absorb through oral buccal mucosa for showing local effect or 2 either it can reach stomach of GI absorption to show systemic effect.

In general composition of chewing gum is mixture of water insoluble phase gum base and some other ingredients which involves

- Powdered sugar which give brittleness to chewing gum
- Corn syrup/glucose act as a humectant and coat the sugar particle to stabilize them.
- Softeners.
- Food colourant.
- Preservative.
- Flavour ants

There are various methods now a days for manufacturing of chewing gum. A proprietary technology for directly compressible gum base have been developed which led to formulation of product using a conventional facility available in pharmaceutical industry instead of extrusion and it also ensures consistent product and greater manufacturing efficiency. medicated chewing gum are proved to be very important drug delivery system as it meets the high standard of pharmaceutical industry and can be formulated to obtain different release profiles of active ingredient. chewing gum has the ability to retained in mouth for longer period of time and if the drug has the ability to readily absorb from the oral mucosa it will provide fast onset of action for systemic and there would be a potential to avoid the first pass hepatic metabolism. MCG has a good physical property it can be taken easily directly without water and if there is an mishap it can be discontinue immediately.

Physio-chemical properties of the drug like aqueous stability, pKa value, distribution between gum/ saliva, product properties like, composition, mass, manufacturing process and the process of chewing i.e. chewing time, chewing rate, affects the release of drugs from the medicated chewing gum. Varying the formulation and manufacturing process, chewing gum as a drug delivery system can be formulated for an extended period of time.

Advantages[7,8,9]

- High degree of patient compliance especially among children and teenagers
- Ease of administration no required of water
- Prompt termination of therapy in case of any mishap
- Preferred dosage form if local action is desired provide fast onset of action
- If used for systemic has advantage over conventional dosage form by providing protection against first pass hepatic metabolism and against stomach acid.
- Advantageous for patient who have difficulty in swallowing.
- Stimulate flow of saliva in mouth.
- Drugs such acetyl salicylic acid, caffeine show faster absorption through MCG compared to conventional tablet.

Disadvantage of MCG[10,11,12,13]

- There may be risk of over dosage with MCG when compared to other dosage form
- The sorbitol present in MCG can cause diarrhea and flatulence
- Prolong chewing of gum can may lead to pain in facial muscle
- Not every drug can be formulated into the chewing gum
- Additives in gum like flavouring agent,
- Cinnamon can cause ulcers in oral cavity and liqorice cause hypertension.

Composition of GUM[14,15]

1. Gum base

Gum base is an insoluble, inert and non-nutritional compoind used as a supporting agent for the edible and soluble of the chewing gum (glucose, sugar, polyols and flavors)

2. Elastomers

These includes natural as well as synthetic rubbers. Gum base is composed of elastomer and solvents that help to soften the elastomer base substance. Elastomer solvents comprises of terpinene resins such as polymers of alpha-pinene or beta-pinene, methyl, glycerol pentaerythritol esters of resins or modified resins and gums, such as hydrogenated, dimerized or polymerized resins or mixtures. The quantity of elastomer solvents used may vary from 5.0% to 75.0%, the weight of the Gum-base, and it's preferred range is from 45.0% to 70.0%, by weight of the Gum-base. Synthetic-elastomers including butadiene, styrene copolymers, polyisobutylene, copolymers, polyethylene mixtures, and, such as polyvinyl alcohol used widely. The molecular weight of the vinyl polymer ranges from 3,000 to 94,000. The quantity of gum base used changes greatly which depends on factors such as the type of base used, consistency of the gum desired and other excepients used in the Chewing Gum preparation. Generally, the amount of gum base will be from 5% to 94%, by weight of the final chewing gum composition. Preferably, the gum-base is used in quantity from 15% to 45% and more preferably in amounts from 15% to 35% by weight of the final chewing gum composition.

3. Plasticizers

vegetable oils, waxes, glycerides. Plasticizers/softeners are polyurethane waxes palmitic acid, oleic acid, stearic

acid, lanolin, sodium stearate, glyceryl triacetate, glyceryl lecithin, glyceryl monostearate, potassium stearate propylene glycol monostearate, acetylated monoglyceride, glycerine, natural and synthetic waxes, hydrogenated vegetable oils, paraffin waxes, microcrystalline waxes, fatty waxes, sorbital monostearate, propylene glycol, are incorporated in the gum-base to obtain diffferent desired textures and consistency.

4. Adjuvants

Talc, calcium carbonate, or other charging agents are used. Mineral adjuvants includes calcium carbonate, magnesium carbonate, aluminum hydroxide, aluminum silicate, talc, tricalcium phosphate, dicalcium phosphate serve as fillers and textural agents.(Volume-1/Issue-1/July-August 2011)

5. Antioxidant

An anti- oxidant such as butylated hydroxytoluene, butylated hydroxyanisole, propyl gallate, are incorporated as antioxidants.

6. Compression adjuvants

Compression adjuvant such as magnesium stearate, silicon dioxide,calcium stearate and talc are used in medicated chewing gum for easy compression. Alkaline earth metal phosphates and alkali metal phosphates avoids caking as well as balling of "High" i.e. 2 to 8% moisture- containing chewing gum compositions during grinding. It has been established that maltodextrin improves the grinding of "high" moisture containing chewing gum by absortption of moisture that allowd lubrication of the gum as it separates into granules. In case of oily lubricants, it is preferred to be 0.4% to 1% by weight of the tableted chewing gum composition.

7. Glidant

Used in the chewing gum (tablet form) composition is from 0.5% to 5% by weight of Chewing gum tablet. These glidants are selected from the group consisting of alkali metal salts, talc, starch, polyhydric alcohols and mixtures.

8. Antiadherent

These are used to to prevent tablet granulations from sticking to the punches and the die walls and also to prevent adherence of chewing gum granules from adhering to one another by a phenomenon known as blocking. Anti- adherents can be added to the chewing gum composition directly into the hoppers, or subsequent to grinding, and are selected from the group consisting of silicates, silicon dioxide, talc and mixtures .Generally anti-adherent is a finely divided low bulk density powder, which is preferably water insoluble. The most preferable anti-adherents are fumed silica and talc. The term-fumed silica include pyrogenic silicas, micron sized silicas and hydrated silicas.

9. Sweetners

a) Water soluble sweetener: xylose, ribulose, glucose, mannose, galactose, fructose, sucrose, maltose, steviosides glycyrrhizin, and sugar alcohols such as sorbitol, mannitol, hydrogenated starch hydrolsates.
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 phyenylglycerine.
d) Water soluble sweeteners: usuallly derived from naturally occurring water soluble sweeteners, chlorinated derivatives of ordinary sugar (sucrose, known as Sucralose)
e) Protein based sweeteners: such as thaumaoccous danielli (Thaumatin I and II) is utilized to provide the level of sweetness desired, and this amount will differ with the sweetener selected and are present in amounts from 0.0025% to 90% by weight of the gum composition.

10. Coloring agents

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

11. Flavouring agenst

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

Manufacturing processes

These are the three main methods for manufacturing of MGCs.

1. Conventional/ traditional Method (Melting)[16]
2. Freezing, grinding and tabletting Method
3. Direct Compression Method

Conventional method procedure[16]

Constituents of gum base are softened or melted and mixed with sweeteners, syrups, active ingredients in a kettle mixer and other excipients are added at a definite time. The gum is then passed 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 also done to prevent the gum from sticking and to make it more flavourant. In a carefully controlled room, the gum is cooled for up to 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) Not suitable for thermolabile drugs at high temperature.
2) Melting and mixing of highly viscous gum mass creates difficulty in controlling of accuracy and uniformity of drug dose.
3) Difficult to make precise form, shape or weight of dosage form.
4) Lack of technology 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.

Cooling, grinding and tableting method[18]

This method has been requried to lower the moisture content and eliminate 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 remain brittle) during the subsequent grinding step without adhesion to the grinding apparatus. The temperature decided for cooling is determined in part by the constituent of the CG and is easily determined by observing the properties of the cooled chewing gum composition. Normally the temperatures of the refrigerated mixture are around -15ºC or lower. The refrigerated composition is then crushed or ground to get minute fragments of finely ground pieces of the composition. For productive cooling, the chewing gum constituents can be pre cooled prior to cooling to the refrigeration temperature. Sometimes a mixture of chewing gum constituents, solid carbon dioxide and precipitated silica is ground in a mill grinder in a first grinding step. Supplementary solid carbon dioxide and silica are added to the ground composition, and the composition is extra ground in a second grinding step. This two step grinding process conveniently keeps the chewing gum constietuent at a very low temperature. The solid carbon dioxide is also added to increase the efficiency of the grinding process. An anti-caking agent like precipitated silicon dioxide can be mixed with chewing gum constituent and solid carbon dioxide before grinding. This stop agglomeration of the afterwards ground chewing gum particles. To avoid the gum from sticking to the grinding apparatus, 2-8% by weight of grinding aid like alkaline metal phosphate, an alkaline earth metal phosphate or malto dextrin can be added. However practical use of these substances is restricted because these substances are more alkaline and therefore incompatible with acidic ionisable therapeutic agents. This gives a chewing gum product that is light and soft chewing feeling when chewed.

Tableting

Once the coolant has been withdraw from the powder, the powder can be mixed with other ingredients such as binders, lubricants, coating agents and sweeteners etc, all of which are suitable with the constituents of the chewing gum base in a appropriate blender such as sigma mill or a high shear mixer. Alternatively a Fluidized Bed Reactor (FBR) can be used. The use of FBR is beneficial as it partially rebuilds the powder into granules, as well as coats the powder particles or granules with a coating agent and minimize unpleasant particle agglomeration. The granules so obtained can be mixed with antiadherents such as talc. The mixture can be blended in a V type blender, screened & staged for compression. Compression can be done by any conventional process such as punching. It needs equipment apart from conventional tabletting equipment and needs cautious monitoring of humidity at the tabletting process.

Need of directly compressible chewing gum excipients[19]

The manufacturing process can be enhanced if a directly compressible chewing gum excipient is present. The restrictions of melting & freezing can be prevent by the use of these. PHARMAGUM® is one such compactable gum system made by SPI Pharma. Pharmagum is a mixture of polyol(s) and sugars with a chewing gum base. It is available as directly compressible powder, free flowing powder which can be compacted into a gum tablet with the help of 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). 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. Release of nicotine from directly compressible nicotine gum formulations and from Nicorette® made by conventional methods has shown that use of Pharmagum in formulation showed a increase release rate. Formulations made with Pharmagum® M & S are similar to tablet in appearance. 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 based on time of contact of MCG in oral cavity. In clinical trial chewing time of 30 minutes was considered close to ordinary use.[20]

2. Physicochemical properties of active ingredient

Physicochemical properties of active ingredient shows 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 release from MCG is affected by chewing frequency and chewing intensity which is different in every person. In-vitro study prescribed by European Pharmacopoeia suggest 60 cycles per minute chewing rate is required for release of active ingredient.[21]

4. Formulation Rate of release of active ingredient is affected by constituent and amount of gum base. Release rate can be decreased by increasing the lipoophilic fraction of gum and vice versa.

Evaluation of MGCs

1. Uniformity of content[20,22]

Unless otherwise prescribed or justified and authorised, MGCs with a content of active ingredient less than 2 mg or less than 2 per cent of the total mass comply with test A for uniformity of content of single-dose preparations. If the preparation contains more than one active substance, the requirement applies only to those active substances which correspond to the above conditions.

2. Uniformity of mass[23]

Uncoated MGCs and, unless otherwise justified and authorised, coated medicated chewing gums comply with the test for uniformity of mass of single-dose preparations. If the test for uniformity of content is prescribed for all the active substances, the test for uniformity of mass is not required.

3. In-vitro drug release

It has been reported commercially that the drug release from MGCs as per the specification given in European Pharmacopoeia and determined by applying a mechanical kneading procedure to a piece of gum placed in a chewing chamber containing a known volume of buffer solution.

Apparatus I Compendial chewing gum apparatus [24]

The chewing apparatus for MGC was adopted by Ph. Eur. in 2000

The chewing apparatus comprises

1. chewing chamber
2. horizontal pistons,
3. vertical piston (tongue).

The vertical piston operates alternatively with the two horizontal pistons and makes sure the gum stays in the right place between chews. If necessary, it is feasible to construct the machine so that at the end of the chew the horizontal pistons rotate around their own axes in opposite directions to each other to obtain maximum chewing. Kinjal R. Shah et al /Int.J.Pharm Tech Res.2014,6(1),pp 35-48.

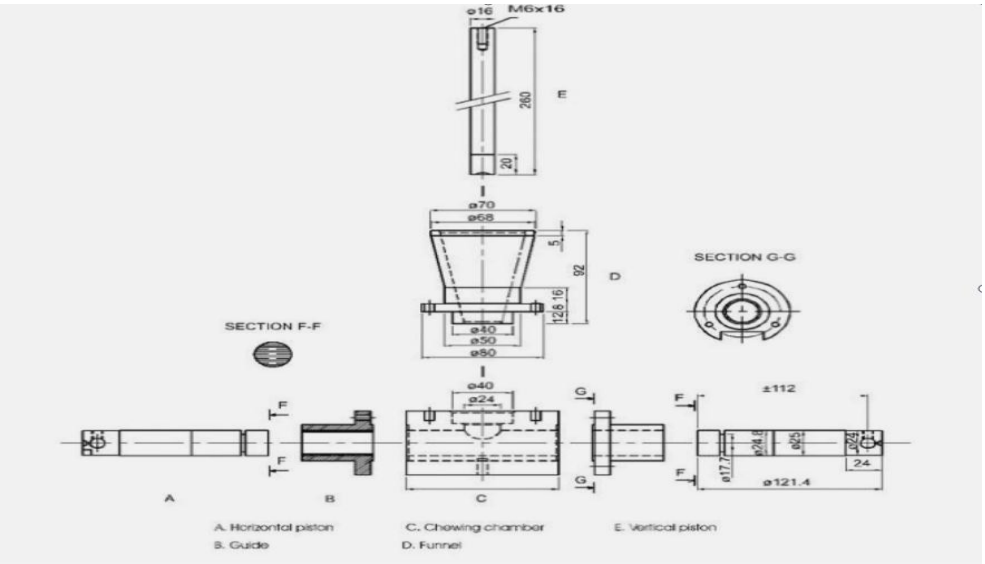

Figure no 1: Compendial chewing gum apparatus.

Apparatus II Noncompendial chewing gum apparatus[25,26] One l apparatus commercially available was designed by Wennergren 26. The representation of the Wennergren chewing apparatus is shown in Figure 3.

Procedure

The chewing procedure consists of reciprocations of the lower surface in combination with a shearing (twisting) movement of the upper surface that provides mastication of the chewing gum and at the same time adequate agitation of the test medium. The upper jaw has a flat surface that is parallel to the central part of the lower surface. The small brim of the lower surface is angled upwards (45 degrees) so that the lower surface functions as a small bowl with a flat bottom. This bowl prevents the chewing gum from sliding during mastication.

The in vivo release of active ingredient from chewing gum can be studied by recruiting a panel of sufficient numbers of tasters and scheduled chew-out studies. For

the duration of the chewing process the drug present within the MCG is released in the saliva and then it is either absorbed through oral mucosa or, if swallowed, it is absorbed through the GI tract.

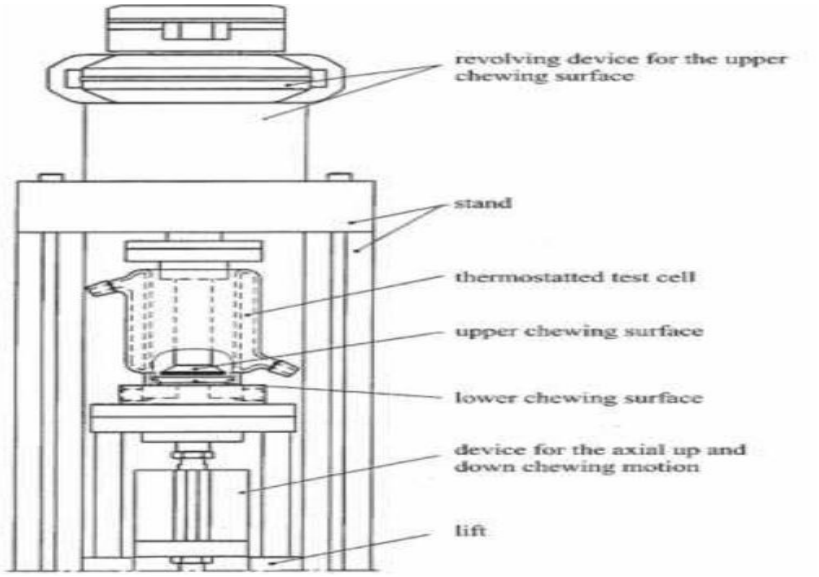

Figure No 2: Noncompendial chewing gum apparatus.

4. In vivo chew out study[29]

The volunteers is asked to chew the drug delivery device for a certain period of time and to assess the remaining quantity of active substance in the residual gum. In this way, the gums are really chewed and the formulation is subjected not only to the mechanical stresses of an artificial machine but also it undergoes all the phenomena involved in this process (increase of salivary secretion, saliva pH variation, swallowing and absorption by the oral mucosa, etc.) which can strongly influence the performance of the dosage form as well as the amount and rate of drug release. Optimized formulation with good consistency can be selected for there lease of drug in the saliva.

Minimum four human volunteers can be selected (two male and two female). should rinse their mouth with distilled water allowed to chewing the medicated chewing gum for 15 minutes, for maximum release has to be taken Sample of saliva are taken after 2, 4, 6, 8, 10, 12, 14 and 15 minutes. samples are diluted in required solvent and absorbance is measured using suitable analytical method. Kinjal R. Shah et al /Int.J.PharmTech Res, 2014; 6(1): pp 35-48.

5. Dissolution test of residual MGCs[27]

In this experiment, gums are tested by a panel of volunteers to verify the drug release process from the drug delivery system.

Each volunteer chews one sample of the tableted gum for different time periods (1, 5, 10 and 15 minutes).

The residual gums are cut into small pieces frozen and then ground till obtaining a fine powder The residual drug content is determined by using suitable analytical method.

The amount of drug released during mastication is calculated by subtracting the amount of residual active ingredient present in the gum from the total content, where as pharmacokinetics can be determined from withdrawn blood samples at specific time intervals. The prerequisites of human volunteers, person-to-person variability in the chewing pattern, chewing frequencies, composition of individual salivary fluid and flow rate of saliva are a few limitations of chew-out studies.

6. Urinary excretion profile[28]

Only applicable to drugs which are excreted via urine. minimum four healthy human volunteer are selected for the study. Volunteers are strictly instructed that they should not take any medicine in the last 48 hours. They are fasted overnight, and emptied their bladder in the volumetric flask. Sample collection starts from blank of zero hour urine. Then sample collection is done on 15 minutes, 1, 2, 3, 4, 6, 7, 8, 10, 11, 12 and 24 hour intervals after administration of medicated chewing gum. volunteers should drink water at regular intervals of 30 minutes. urine samples are analyzed by suitable analytical methods.

7. Buccal absorption test

Human volunteer swirled fixed volume of drug solution of known concentration at different pH value of 1.2, 5, 6, 6.5, 7, 7.5, 7.8, 8.0, in the oral cavity for 15minutes and then expelled out. saliva is analyzed for drug content and back calculated for buccal absorption.

8. Texture analysis

Texture studies by instrument Instrumental texture analysis is mainly concerned with the evaluation of mechanical characteristics where the mcg is subjected to a controlled force from which a deformation curve of its response is generated. For evaluating texture properties

of MCG a "compression" probe was used in this deformation method by using the texture analyzer. Squashing solid and self-supporting samples enabled a number of textural properties to be evaluated, including hardness (peak force that results from a sample being compressed to a given distance, time, or % of deformation) and adhesiveness (stickiness-related to how a MCG adheres to the inside of the mouth surfaces during chewing). It is recommended to use a compression probe with a greater surface area than that of the sample being tested, so a compression platen probe of 50 mm ø was used. During evaluation, a constant force should be applied on the surface of self-supporting MCG and upon fracture it should be withdrawn. Through which, a deformation curve can recorded and interpreted.

Texture studies by human volunteer

For assessment of the product quality, volunteers should the product without swallowing for a particular time period. Then, they are allowed to give their experience that they felt appropriate for respective qualities of MCG product, i.e. product feel, product consistency, its taste, and total flavor lasting time during chewing the product.

Application of medicated chewing gum

The MCGs are also used alternatively as a tool to buccal tablets and sublingual tablets. They act both locally and systemically since the drug is released more uniformly and also covers maximum absorption are in the oral cavity.[18] MCGs are majorly used for local effects in certain conditions (anti-plaque, fresh breath, dental caries, plaque acid neutralization, fungal, and bacterial infections) and systemic effects in certain conditions (vitamin C deficiency, motion sickness, alertness, pain & fever and smoking cessation).[19] Various applications of mediated chewing gum are stated below.

(A) Local Therapy[30]

The main objective of medicated chewing gum is to prevention or treatment of oral diseases. From this formulation, the active drug material gets released in a controlled manner and shows local action against dental caries. Low plaque pH shows substantial role in the cause of dental caries. Hence, sugar-free chewing gum is suggested after meals for prevention of such dental caries.

1. Dental Caries[31]

- To prevent as well as cure oral diseases by acting at the main target site.
- To achieve controlled release rate of active drug substances and to provide a extended local effect.
- Lowers frequency and intensity of dental caries by increasing the plaque pH.
- Fluoride chewing gum can be used to avoid dental caries in children.
- Chlorhexidine chewing gum can be used to treat several infections (periodontitis, gingivitis, oral and pharyngeal infections) and cause fewer staining of teeth.
- Taste masking of bitter tasting drugs such as Chlorhexidine.
- Drugs soluble in saliva are released immediately.
- Lipid soluble drugs are released slowly.
- The local/systemic effect depends on the contact time of MCG in oral cavity.
- Since different individual chews the gum diffirently the release of active drug substance may vary from person to person.
- The release rate of active drug substance mainly depends upon composition and amount of gum base used.

(B) Systemic Therapy[32]

MCG formulations offer improved absorption through the buccal mucosa after systemic drug delivery. Systemic therapy of MCGs can be used in the treatment of children, adults and adolescents due to its numerous advantages such as quick action, ease in administration, no need for water, MCGs are advantageous in number of indications such as:

1. Pain[33]

- Chewing gum formulation containing NSAIDS can be used for treatment of minor pains, headache and muscular aches.
- Example of such formulation is Aspergum®, a chewing gum containing ASA (aspirin or acetylsalicylic acid).

2. Smoking Cessation[34]

- Nicotine, silver acetate and lobeline containing formulations have been proven clinically to help in smoking termination. Aslani and Rafiei (2012) prepared nicotine containing chewing gum by direct compression method to help smokers quit smoking. The final formulation had optimal chewing hardness, adherence to teeth, pleasant taste and highest acceptability to smokers
- Nicotine chewing gum is considered as a convenient formulation for breaking an "oral habit" such as smoking.

3. Obesity[35]

- Substances like Guarana and caffeine containing preparations are shown to be efficient in managing obesity.
- Caffeine and Guarana have shown to increase the metabolic rate and stimulate lipolysis along with reduced feeling of hunger.

Aslani and Jalilian (2012) formulated caffeine containing chewing gum to increase alertness and decrease fatigue

Table No 1: Marketed prodcut of medicated chewing gum.[36,37,38]

Active Ingredient	Uses
Chlorhexidine	Prevention of dental caries
Aspirin	Analgesic
DHA, CCE	Enhanced brain activity
Guarana	Alertness
Caffeine	Alertness

Future Opportunities

Chewing gum offers clinical benefits along with being attractive, discrete and an efficient drug delivery system. Presently various diseases can be treated with Novel Drug Delivery Systems. In general, it can take time for a Novel drug delivery system to prove itself in the market and gain acceptance and popularity among patients, however chewing gum has proven to show its position as a suitable and beneficial drug delivery system as it meets the high quality standards of pharmaceutical industry which can be formulated to achieve different release profiles of active drug substances. Finally, in several years, we may see that more drug are formulated in form of chewing gum as preferred to other delivery systems to deliver drugs locally to the oral cavity. The reason being that the chewing gum delivery system is convenient, can be easily administered anytime and anywhere, and its pleasant taste increases the product acceptability and patient compliance.

CONCLUSION

MCGs is most convenient, self medicated, easily administered without water and highly patient compliant.

It's capability to allow local and systemic delivery of drug makes it preferable over other delivery system. Thus in upcoming years it is sure that the medicated chewing gum would be most popular drug delivery system.

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