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Review Article

An Updated Review on Medicated Chewing Gum

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ABSTRACT

Chewing gums are mobile drug delivery systems. It is a potentially useful means of administering drugs either locally or systemically via, the oral cavity. The medicated chewing gum has through the years gained increasing acceptance as a 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. In addition, a large number of chewing gum intended for prevention of caries, xerostomia alleviation, and vitamin/ mineral supplementation are currently available. Today improved technology and extended know how have made it possible to develop and manufacture medicated chewing gum with predefined properties. MCGs (Medicated chewing gums) are solid, single dose preparations with a base consisting mainly of gums that are intended to be chewed but not swallowed. They contain one or more active substances which are released by chewing and are intended to be used for local treatment of mouth diseases or systemic delivery after absorption through buccal mucosa. The present review article is nicely discussed advantages, disadvantages, formulation, manufacturing process, limitation of manufacturing process, factors affecting release of active substance, quality control tests for chewing gum, significance, stability study and future trends in chewing gum drug delivery system.

Keywords: Chewing tablet, gum, medicated gum, elastomer, Novel Dissolution apparatus, dental caries.

INTRODUCTION

Chewing gum is being used worldwide since ancient times after man experienced the pleasure of chewing a variety of substance. One thousand years ago the Mayan Indians chewed tree resin from the sapodilla tree in order to clean their teeth and freshen their breath. Shortage of natural gum bases during World War II enhanced development of the synthetic gum bases that are used today. Chewing gum can be used as a convenient modified release drug delivery system. Medicated chewing gums are currently available for pain relief, smoking cessation, travel illness, and freshening of breath. In addition, a large number of chewing gum intended for prevention of caries, xerostomia alleviation and vitamin / mineral supplementation are currently available. The first commercial chewing gum "State of Maine pure spruce gum" was marketed in 1948 in the U.S.A. The first patent was filed in 1869. The gum was intended as dentifrices but it has never been marketed. The first Medicated chewing gum "Aspergum" was launched in 1928. This chewing gum is still available and contains acetylsalicylic acid. Another commercially available medicated chewing gum is dimenhydrinate – containing chewing gum for motion sickness. However, chewing gum did not gain acceptance as a reliable drug delivery system until 1978, when nicotine chewing gum became available. Today improved technology and extended know how have made it possible to develop and manufacture medicated chewing gum with pre-defined properties. Consequently, today chewing gum is aconvenient drug delivery system, which is appropriate for a wide range of active substances. Medicated chewing gum offers advantages in comparison to conventional oral mucosal and oral dosage forms both for (a) local treatment (b) systemic effect after absorption through the buccal and sublingual mucosal and from the gastrointestinal tract. Chewing gum can be retained in the oral cavity for a long period and, if the drug is readily absorbed across oral mucosa, chewing gum can provide a fast onset time for a systemic effect and the potential for avoidance of gastrointestinaland hepatic first – pass metabolism of susceptible drugs.

Generally, medicated chewing gum has a good stability, the medicine can be taken easily and directly without the prerequisite of water, and if required, prompt discontinuation of medication is possible. Physiochemical 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, chewingrate, 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.

CHEWING GUM DOSAGE FORM FOR BUCCAL DELIVERY

Dosage forms such as mouthwashes, erodible/ chewable buccal tablets, and chewing gums allow release of drugs for only a short period and thus the reproducibility of drugs absorption is comparatively poor. Application of bioadhesive semisolid gels creates considerable technical problems in the buccal absorption. Although medicated chewing gums pose difficulties in regulating the dose administered, they still have some advantages as drug delivery devices, particularly in the treatment of diseases in the oral cavity and in nicotine replacement therapy. Some commercially available chewing gums are Caffeine chewing gum, (Stay Alert®,) and Nicotine chewing gums(e.g. Nicorette ® and Nicotinell®). The permeability of nicotine across the Buccal mucosa is faster than across the skin. However, chewing gum slowly generates a steady plasma level of nicotine rather than a sharp peak as experienced when smoking. Possible swallowing of considerable amount of nicotine during chewing may lead to decreased effectiveness of the chewing gum due to first pass metabolism and gastrointestinal discomfort. It is a major challenge to optimize the dose-response relationship of nicotine administered in a chewing gum.

ADVANTAGES

1. Convenient – promoting higher compliance
2. Discreet- less stigmatization
3. Administration without water can be taken anywhere
4. Excellent for acute medication
5. Advantageous for patients with difficulty in swallowing tablets
6. Pleasant taste
7. Counteracts dry mouth: Through stimulation of the salivary secretion thereby preventing.
8. Candidacies and caries.
9. Highly acceptable by children
10. The active compounds absorbed at oral level avoid the hepatic circulation andthe associated metabolism.
11. The product is rapidly released from the gum after a short period mastication;some absorption takes place by directly through the oral mucosa depending onthe active ingredient. Importantly not being swallowed the gum does not reachthe stomach. Moreover, the stomach does not suffer from direct contact withhigh concentrations of active principle, this reducing the risk of intolerance ofthe gastric mucosa.
12. The fraction of product reaching the stomach is conveyed by the saliva anddelivered continuously and regularly. Active substances are released frommedical chewing gum during chewing and are dissolved in saliva. The releaserate can be carefully controlled through the formulation of the chewing gumallowing extendedexposure in the oral cavity. Active substances that areabsorbed through the buccal mucosa pass via the jugular veins directly into thesystemic circulation. Due to the rich vascular supply of the buccal mucosa,measurable concentrations of active substances may be in the blood after onlya few minutes of chewing and fast onset of action is thus likely to be attained.Furthermore, bioavailability may be increased, as hepatic first passmetabolism and gastrointestinal tract degradation are tract degradation areavoided for buccal-absorbed substances.
13. Consequently, a lower dosage of substance may be therapeutically sufficient,possibly resulting in a fewer side effects, and promote fast absorption. Activesubstances released from chewing gum are dissolved in saliva whenswallowed and are, therefore, readily accessible for absorption in thegastrointestinal tract.

MANUFACTURING

1. **Gum Base**-Gum base is an inert and insoluble nonnutritive product used as asupport for the edible and soluble of the chewing gum (sugar, glucose, polyoils and flavors) other raw materials are generally grouped in the followingclasses:
2. **Elastomers**: including natural and synthetic rubbers. The gum basecomposition may contain conventional elastomer solvents to aid in softeningthe elastomer base component. Such elastomer solvents may

compriseterpinene resins such as polymers of alpha-pinene or beta-pinene, methyl,glycerol or pentaerythritol esters of resins or modified resins and gums, suchas hydrogenated, dimerized or polymerized resins or mixtures. The elastomersolvents may be employed in amounts from 5.0% to 75.0%, by weight of thegum 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 vinylpolymer, such as polyvinyl alcohol are widely used bases. The molecularweight of the vinyl polymer may range from 3,000 to 94,000. The amount ofgum base employed varies greatly depending upon various factors such as thetype of base used, the consistency of the gum desired and the othercomponents used in the composition to make the final chewing gum product.In general, the gum base willbepresent in amount from 5% to 94%, by weightof the final chewing gum composition. Preferably, the gum base is used inamounts 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 suchas lanolin, palmitic acid, oleic acid, stearic acid, sodium stearate, potassiumstearate, glyceryl triacetate, glyceryl lecithin, glycerylmonostearate,propylene glycol monostearate, acetylated monoglyceride, glycerine, naturaland synthetic waxes, hydrogenated vegetable oils, polyurethane waxes,paraffin waxes, microcrystalline waxes, fatty waxes, sorbitalmonostearate,propylene glycol, may be incorporated into the gum base to obtain a variety ofdesirable textures and consistency properties.
4. **Adjuvants**: calcium carbonate, talc, or other charging agents are used.Mineral adjuvant such as calcium carbonate, magnesium carbonate, aluminumhydroxide, aluminum silicate, talc, tricalcium phosphate, dicalcium phosphateserve as fillers and textural agents.
5. **Antioxidants:** An anti- oxidant such as butylatedhydroxytoluene, butylatedhydroxyanisole, propyl gallate and mixtures there of, may be included asantioxidants**.**
6. **Compression adjutants:** Suitable compression adjuvant such as silicondioxide, magnesium stearate, calcium stearate and talc can be used inmedicated chewing gum for ease of compression. The alkaline earth metalphosphates 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 grindingof “high” moisture-containing chewing gum compositions by absorbingmoisture to allow lubrication in the gum as it separates into granules. If oillubricants are used, it is preferred to be 0.4% to 1% by weight of the tabletedchewing gum composition. The amount of glidant present in the tabletedchewing gum composition is from 0.5% to 5% by weight of the tabletedchewing gum composition. Those glidants useful are selected from the groupconsisting of alkali metal salts, talc, starch, polyhydric alcohols and mixtures.Antiadherents function to prevent tablet granulations from sticking to the facesof the punches and the die walls, but most importantly, prevent adherence ofchewing gum granules from adhering to one another, a phenomenon known asblocking. Anti- adherents may be added to the chewing gum compositionwhile the composition is in the hoppers, or subsequent to grinding and areselected from the group consisting of silicates, silicon dioxide, talc andmixtures thereof present in amount of 0.2% to 1% by weight of the tabletedchewing 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 ispreferably water insoluble. The preferred anti-adherents are fumed silica andtalc. The term-fumed silica is meant to include pyrogenic silicas, micron sizedsilicas and hydrated silicas.
7. **Sweeteners**

   a) Water-soluble sweetening agents: xylose, ribulose, glucose,mannose, galactose, fructose, sucrose, maltose, invert sugar partiallyhydrolyzed starch, dihyrochalcones, monellin, 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 suchas Aspartame, Alitame, methyl esters of L-aspartyl-L phyenylglycerineand Laspartyl- L 2,5-dihyrophenylglycine, L-aspartyl 2,5-dihydro-L phenylalanine – L aspartyl – L (1-cyclohexen) alanine.

d) Water-soluble sweeteners: derived from naturally occurring watersolublesweeteners, chlorinated derivatives of ordinary sugar (sucrose,known as Sucralose)

e) Protein based sweeteners: such as thaumaoccousdanielli (ThaumatinI and II) In general an effective amount of sweetener is utilized toprovide the level of sweetness desired, and this amount will vary withthe 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 beincorporated in amounts up to about 6% by weight of the gum composition,titanium dioxide may be incorporated in amounts up to about 2%. Thecolorants may also include natural food colors and dyes suitable for food drugand cosmetic applications.
9. **Flavoring Agents:** Flavoring agents suitable for use are essential oils andsynthetic flavors such as citrus oils, fruit essences, peppermint oil, spearmintoil, clove oil wintergreen oil, and anise oil.

PROCESS FOR PREPARATION

Different authors have reported various processes of preparation of medicatedchewing gum, that are mentioned as under:

1. Formation of a inclusion complex, which is dried and mixed granulated gumbase without adding water or other solvents. The process is carried out atcontrolled temperature and humidity and the blended components are coldpressed to produce a final gum product. Attempts have been made toincorporate pharmaceutically active agents into chewing gum as means ofadministering the active agent to the subject. Traditionally, these efforts haveemployed common chewing gum production techniques wherein a gum base isheated until it becomes viscous or fluid mass. Additional components (such asflavors or active ingredients) then are blended into gum base. Finally, themixture is cooled, pressed and cut to produce the final product.
2. Alternatively, various components are blended in gum slurry that is coagulatedbefore pressing into the final product form.
3. To avoid the degradation of the active agents, coldproduced chewing gum bydirect compression of the ingredients has been tried so as to retard or controlthe release rate of active agents along with the microencapsulated activeagents.

PROBLEMS ASSOCIATED WITH ABOVE METHODS

1. Many pharmaceutically active agents possess unpleasant taste or odor thatresults in the undesirable chewing gum products. Many active agents also tendto irritate the mucosa and few others degrade rapidly, making impractical toinclude them in chewing gum.
2. Another problem associated with the above methods is that the gum base isheated to a fluid mass to facilitate mixing of other ingredients. Such elevatedtemperatures can cause degradation of heatsensitive compounds, includingactive agents and flavors.
3. Further, medicated gum preparations often utilize organic solvents to dissolvethe active agents, it is difficult to eliminate these organic solvents from thefinal product and may present certain health risks if even trace amounts remainin the final dosage forms.
4. Additionally use of organic solvents in connection with industrial processes isbecoming increasingly unpopular due to health and environmentalconsiderations (e.g. risks attendant to exposure of personnel and problems ineffecting proper disposal of waste solvents).
5. Water can also be utilized in gum preparations but it is difficult to eliminate,especially at the relatively low temperatures that are desirable for productionof chewing gum. Heating the gum mass to eliminate water is not advisable,because the gum will then become stickier which makes handling difficult andinterferes with large scale, semi-or totally automated production. Conventionalchewing gum compositions are

difficult to form into chewing gum tabletsbecause of their moisture content. Traditional chewing gum compositionscontain 2% to 8% by weight of water.

6. Generally the chewing gum will jam the grinding machine, sticking to blades,screens and other surfaces if moisture level is not controlled. Traditionalmoisture levels can cause caking and balling of the gum during granulationprocess thereby preventing the formation of gum granules that are necessaryfor tableting. Alternatively, if moisture content is greater than 2% by weight,various other problems can occur, e.g. adherence to the punch press,compaction in the punch press hopper, poor low in the feeder section anddifficulties with compressibility. Thus the problems of realizing a medicatedchewing gum produced by direct compression with immediate or rapid releaseof the active agent and efficient masking of unpleasant organolepticcharacteristics of active agents remain unsolved. In view of the deficiencies ofthe prior methods of producing medicated chewing gum containing activeagents a process has been reported that overcomes these various shortcomingsand provide a novel process for producing medicated chewing gum containinginclusion complexes of cyclodextrins and active agents. This process avoidsthe use of organic solvents and water and is especially adapted for use withheat sensitive active agents. Further, it avoids the heated gum base and slurriestoo. The novel method that has been patented includes cooling the gum basegrinding it into granules, which are then dry-mixed with optional excipients inthe absence of water and solvents at controlled temperature and humidity,cold- pressing the mixed gum and components into the final product. Thehydro-soluble and lipid soluble active agent are encapsulated in cyclodextrinsand are liberated in the mouth by saliva amylases. By inclusion incyclodextrins, the active agents are stabilized and are made more soluble. Thewell-developed technology used for generating the inclusion complexes issimpler and advantageous when compared to that of micro encapsulation.

Furthermore, through the use of the inclusion complexes, the bioavailability ofthe cyclodextrinencapsulated active agents is accentuated. In addition thistechnique provides an excellent means of masking the unpleasant organolepticcharacteristics of many active agents. One or more well-known chewing gumexcipients can be added to the gum base before or after combining it with theinclusion complex. The powder containing the inclusion complexes ofcyclodextrin and active agent is mixed with the processed gum base in theabsence of water or organic solvents. The ratio between the inclusion complexand the processed gum based can vary widely depending on the amount ofactive agent that should be delivered. The medicament is added to the gumgranules along with the compression aid, pharmaceutical drugs or other activeagents are added in a number of formsincluding encapsulated, but they areprefereably added in a dry state. Active agents may themselves be granulatedand added in this form to the tableted chewing gum composition. Liquidwater-soluble drugs can be added to a solution of modified malt dextrin andspray dried. Liquid, oil soluble drugs and active agents can be blended withthe compression aid components prior to mixing with the gum granules, theliquid drug or active agent should not exceed more than 30% by weight. Theadvantage of the tableted gum composition as a means for dispensing drugsmedicaments and other active agents is that the component is trapped betweengranules and not within the gum composition. Hence, it is readily bioavailableand nearly completely released upon chewing of the gum.

STABILITY

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

QUALITY CONTROL

As per specifications given in European Pharmacopoeia.

1. **Test for Uniformity of Content:** Unless otherwise prescribed or justified andauthorized medicated chewing gum with

content of 2 mg or less than 2 percentof the total mass of gum comply with test.

2. **Uniformity of mass:** Uncoated medicated chewing gum and unless otherwisejustified and authorized coated medicated chewing gum comply with the testfor uniformity of mass of single- dose preparations.
3. **Drug release from medicated chewing gum:** It has been reportedcommercially that the drug release from medicated chewing gum as per thespecification given in European Pharmacopoeia and is determined by applyinga mechanical kneading procedure to a piece of gum placed in a small chewingchamber containing a known volume of buffer solution.

FACTORS AFFECTING RELEASE

The release rate of an active substance is determined not only by the formulation ofthe chewing gum but also by the properties of the active substance and of theindividual chewing the gum. The chewing gum – The water content of gum base isvery low and the gum binds lipophilic substances very firmly. In order to obtain theoptional formulation it is possible to

1. Decrease the release rate of highly hydrophilic substances
2. Increase the release rate of lipophilic substances
3. Achieve a more complete release of lipophilic substances
4. Prolong the release
5. Changing the water solubility of the active substance will increase or delay therelease.

Asimilar effect may be obtained by changing the hydrophilic/lipophilic balance of thechewing gum formulation. The simplest way of achieving this is to increase ordecrease the amount of gum base. An increase in the gum base will make theformulation more lipophilic and thus reduce the release rate of a given active substance. In principle, it is possible to manufacture products with a very low gumbase content, but in practice a portion of chewing gum containing less than 20% gumbase will have inferior chewing properties and may not be considered a viableformulation. Instead of changing the gum base content, it is far more effective tochange the release properties by adding solubilizers to the formulation. This methodenables release from the chewing gum of even highly insoluble substances, e.g.Miconazole. However using solubilizers requires specially designed gum bases as thesolubilizer affect the texture of chewing gum. This may result in residual productbecoming soft to an unacceptable degree after a very short period of chewing. Othermethods are available for instance nicotine can be formulated as complex bound to acation exchange resin leading to a prolonged release. This ion exchange principlecould of course, also be used for other ionic substances. It is also possible to granulatethe active substance with hydrophilic components, melted lipids, or to mix the activesubstance with a melted polymer.

6. **The active substance:** The release rate of an active substance depends on thesolubility of the active substance in water and saliva. Highly hydrophilic substancewill be almost completely released within 10 to 15 minutes. Substances withsolubility in water or less than 0.1 – lg/100ml are lipophilic components of the gumbase and thereby show a slow and incomplete release. Active substances may befound in the form of salts or compounds with different solubilities, e.g. pro-drugs,thus the compound offering the best properties for achieving optimal release may beselected. Chlorhexidine can serve as an example apart from pure chlorexidine,chlorhexidine is available as different salts with different solubility. A specialcompound or pro-drug may be obtained by formulating a complex with an activelipophilic substance, e.g. by using cyclodextrines. This will result in a compound withhigher water solubility and consequently increased release. It is also possible toincrease or delay the release of an active substance by changing the physical formthrough a variety of coating and encapsulating techniques of the substance particles.A hydrophilic or a hydrophobic coating may encapsulate the active substance. Toreduce the release rate a coating with ethyl cellulose can be used.
7. **The individual:** For medical chewing gum as for other pharmaceutical products isan inter-patient variance. Additional to conventional pharmaceutical formulations,other inter-patient variations apply for a chewing gum formulation. When theindividual is chewing the gum it may be regarded as an extraction process.Consequently, the release is related to the time the gum is being chewed to thefrequency and intensity by which the individual is chewing, and it depends on theamount and composition of the individual's saliva.

PHARMACEUTICAL SIGNIFICANCE OF MEDICATED CHEWINGGUMS

Prevention and cure of oral disease are obvious targets for chewing gum formulations.Chewing gum can release an active substance at a controlled rate over an extendedperiod of time providing a prolonged local effect.

1. Sugar free chewing gum is known to be beneficial to dental health. It has been shownthat use of sugarfree chewing gum after meals re-elevates plaque. pH plays animportant role in the development of dental caries. Therefore, in caries preventionprograms, sugar-free chewing gum is recommended after meals and snacks as asupplement to tooth brushing.
2. Indications for fluoride chewing are prevention of dental caries in children influoride deficient areas, in adults with a high incidence of caries and in patients withxerostomia.
3. Chlorhexidine chewing gum can be used for alleviations of gingivitis, periodontitisand other oral and pharyngeal infections. It can also be used for inhibition of plaque growth and has proven valuable in oral health care of the elderly. Furthermore,chlorhexidine in a chewing gum formulation gives less staining of the teeth and ismore convenient to use than a chlorhexidine mouth rinse. The chlorhexidine releasedby chewing is distributed evenly in the oral cavity and is present there for aprolonged time. The bitter taste of chlorhexidine can be masked quite well inachieving gum formulation.
4. Clinical trials involving patients with oral candidia sis have shown that miconazolechewing gum is at least as efficient as miconazole oral gel in the treatment of fungalinfections in the mouth. Furthermore, patients preferred chewing gum to oral gel dueto convenience and fewer side effects.
5. Chewing gum as a drug delivery system also provides benefits to systemic drugdelivery, especially if the active substance is absorbed through the buccal mucosa,fast and acute treatment, convenience, no need for water and thereby easyadministration – anytime anywhere – reduced risk of gastrointestinal side effects.These benefits apply not only to the treatment of adults, but also to the treatment ofchildren and adolescents. Systemic effect of active substances released from chewinggum can be achieved in two ways. In the “traditional” way by swallowing the activesubstances, or via absorption through the oral mucosa. The latter is of specialinterest, as buccal absorption avoids first-pass hepatic metabolism of the activesubstance, it could provide better bioavailability. Buccal absorption may also lead tofast onset of the action and lead directly in to systematic circulation. Chewing gumpromotes buccal absorption by releasing active substances at carefully controlledrates, thus allowing for extended exposure in the oral cavity.
6. A study of pharmacokinetics of nicotine chewing gum indicated that some of thenicotine was not absorbed through route but was swallowed and underwent first-passmetabolism. It was estimated that approximately 80% of the nicotine released fromthe chewing gum was absorbed through buccal route.
7. Successful treatment of minor pains, headaches, pains of colds, muscular ache, etc.requires rapid absorption of therapeutic doses of active substance. Chewing gum as adrug delivery system could be beneficial in minor pain treatment, when Buccalabsorption results in fast onset of action and reduces the risk of gastrointestinal sideeffects.
8. The bioavailability of acetylsalicylic acid in a chewing gum formulation relative toan unbuffered tablet formulation has been determined. Absorption from the chewinggum formulation was shown to be faster than absorption from the tablet, andconsequently, a chewing gum formulation may provide faster pain relief.
9. Several chewing gum formulations containing caffeine, guarana or chromium areavailable. Caffeine and guarana are central stimulating anorectic agents that havebeen proved to increase the metabolic rate. Moreover, they stimulate lipolysis, have athermogenic effect (increase energy expenditure) and reduce the feeling of hunger.
10. Chromium is claimed to reduce the carving for food due to an improved bloodglucose balance. Chewing gum has been proven efficient in the treatment involvinginstant raving and “oral habits”. Hence there is a rationale for administering weightreducing active substance in a chewing gum formulation.
11. Allergy, nausea, motion sickness, diabetes, anxiety, dyspepsia, osteoporosis, andcough and cold are all indications for which chewing gum as a drug delivery systemcould be beneficial.
12. Chewing gum containing antacids or mucolytics also presents advantages forpatients.

13. Chewing gum as a drug delivery system offers convenience in thetreatment/prevention of motion sickness and nausea. Medicated chewing gumcontaining dimenhydtinate for motion sickness is already on the market, however,active substances like scopolamine, metoclopramide, ondansetron and dolasetronmay be candidates for a chewing gum formulation for the treatment/prevention ofmotion sickness and nausea.
14. Several chewing gum formulations containing calcium are available on the market.Adolescents constitute a potential target group for a calcium chewing gum as thecalcium intake of young people is often very low. Calcium chewing gum with apleasant flavour is an attractive and convenient alternative to tablets.
15. Miconazole has also been formulated as chewing gum and these formulations havebeen used in clinical trials.
16. As Propranolol exhibits first-pass metabolism, a chewing gum formulation was seenas a viable option to obtain buccal absorption.

SAFETY ASPECTS

Generally, today it is perfectly safe to chew chewing gum. Previously, hard chewinggum has caused broken teeth. Extensive chewing for a long period of time may causepainful jaws muscle, and extensive use of sugar alcohol containing chewing gum maycause diarrhea. Long term frequent chewing of gum has been reported to causeincreased release of mercury vapors from dental amalgam fillings. However,medicated chewing gum does not normally require extensive chewing, orconsumption to great extent. Flavors, colour etc. may cause allergic reactions.

Overdosing by use of chewing gum is unlikely because a large amount of gum has tobe chewed in a short period of time to achieve this. Swallowing pieces of medicatedchewing gum will only cause minor release of the drug because the drug can only bereleased from the gum base by active chewing. As a general rule, medicated chewinggum (like other medicines) should be kept out of reach of children, if required; drugdelivery may be promptly terminated byremoval of the gum.

FUTURE TRENDS

Chewing gum not only offers clinical benefits but also is an attractive, discrete andefficient drug delivery system. A few decades ago, the only treatment for somedisease was surgical procedure but now more and more disease can be treated withNovel Drug Delivery Systems. Generally, it takes time for a new drug delivery systemto establish itself in the market and gain acceptance by patients, however chewinggum is believed to manifest its position as a convenient and advantageous drug

delivery system as it meets the high quality standards of pharmaceutical industry andcan be formulated to obtain different release profiles of active substances. Thepotential of MCG for buccal delivery, fast onset of action and the opportunity forproductline extension makes it an attractive delivery form. Reformulation of anexisting product is required for patent protection, additional patient benefits andconservation of revenues.

SUMMARY AND CONCLUSION

Thus, it can be concluded that the chewing gum can be used, as a carrier for vastcategories of drugs where extended release and the local action is desired. Chewinggum can be used without water, at any time. Medicated Chewing gums can produceboth local effects as well as systemic effects in the oral cavity. They can be used forthe purpose of taste masking of certain drugs too.

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