International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 1294-1302 www.ijprajournal.com ISSN: 2249-7781

A Review on Medicated Chewing Gum for Cough

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Submitted: 25-11-2023 Accepted: 05-12-2023

I. INTRODUCTION

1.1 cough

A cough is the rapid expulsion of air from the lungs when the air passages are irritated. Cells within the air passages become irritated by fluids, mucus, or material, and a cough reflex is initiated, forcing air out of the lungs under air mass to clear the irritating substances and protect the lungs. A cough reflex isoften voluntary or involuntary. We reassess the several sorts of coughs and their common causes anddiscuss symptoms youmustn't ignore after youhavea cough.[1]

Types of coughs

A cough is taken into account as 'acute' if it lasts but three weeks and 'chronic' if it lasts longer than eight weeks in adults or four weeks in children. There are various kinds of coughs and therefore the conditions r elated to those coughs canover lap.[1]

Chesty cough

This is referred to as a wet cough or phlegmy cough; this makes a person's chest feel heavy and also the cough brings up mucus or phlegm. Each cough can produce a clump of mucus and thus these styles of coughs are called 'productive coughs. Chesty coughs are caused by viruses from colds and flu and they can happen after an inflammatory disease. Chesty coughs are worse in the mornings as you tend to cough less while asleep, during which period the mucus produced by the cells within the air passages builds up overnight, resulting in excessive coughing and mucus expelling once you get up. Other more serious causes of chesty coughs include asthma, heart condition or bronchitis.[2]

Figure no. 1

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 "As pergum" 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

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 1294-1302 www.ijprajournal.com ISSN: 2249-7781

until 1978, when nicotine chewing gum became available. Extended know how have made it possible to develop and manufacture medicated-chewing gum with pre-defined properties. Consequently, today chewing gum is a convenient 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 gastrointestinal and 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.

Figure no. 2

This is the foremost common sort of cough. it's caused by irritation within the throat and they tend to be the foremost annoying variety of cough non-productive cough because it produces little or nophlegm. Sometimes a post-nasal drip is felt which is caused by inflamed tissue within the nose producing excessmucus, which then drips down into the throat. This post-nasaldriptriggersthecoughreflex.the fore most common causes are colds, flu, hay fever, or coryza. If the symptom is the reason for the ticklycough, then over-the-counter decongestants and antihistamines can help alleviate symptoms.

Dry cough

A dry cough, another non-productive cough, occurs because of irritants within the air passages, and causes can include colds, flu, hay fever, asthma, acid reflux, bronchitis, and certain medications used for treating high pressure**.**

Whooping cough

This can be a heavy infection that causes violent coughing fits. A vaccine against respiratory disease is mostly administered as a part of the vaccination program but the respiratory disorder can spread from non-immunized people to those that haven't yet received the vaccination including young babies. The 'whooping' sound occurs when the kid gasps for breath after a coughing fit. Babies might not cough or make the whooping sound but may gag and gasp.

Choking

Anyone presenting with a sudden episode of coughing or choking should seek immediate medicalattentionifaforeignbodyispresent.Forthepatient'sconvenience, we prepared medicated chewing gum for cough. Due to the acceptance of oral drug delivery systems among people, chewing gums soon became friendly to people all around the world because of their convenient administration. Besides its enjoyable taste and good feeling, it provides proven health, nutrition, and cognitive benefits.[3]

CHEWINGGUM

Chewing gum could be a soft, cohesive substance designed to be chewed without being swallowed. Modern chewing gum consists of gum base, sweetenes, softeners/plasticizers, flavours, colours, and atough or powdered polyol coating. Its texture is paying homage to rubber because of the physical-chemical properties of its polymer, plasticizer, and resin components, which contribute to its elastic-plastic, sticky, chewy characteristics.

History of Chewing gum

Chewinggumcouldbeadrugdeliverysystemthat'svisitingadvancedmoreandmoreinnowadaysresearch. It seems to urge more standardization within the future industry because it can deliver either pharmaceuticals or nutrients referred to as medicated chewing gum (MCG).Ancient Greeks want to get a chewable resin from a tree called mastic but thanks to archaeological diggings chewing gum-like substances or masticatory resins back to 5000 years ago. Resin pieces have even

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been found with teeth traces in Finland and Sweden. The first marketing of chewing gums was in 1848 when chicle from the Manilkara zapota was sapped. John Curtis and his son boiled spruce tree sap and added sugar, flavours and fillers, then rolled it and first made masticator sticks which they wrapped in papers and sold them.

The first MCG was launched in 1924 in the US of America which was called As per gum but an admission of chewing gum as a drug delivery system failed to gain until nicotine chewing gum was released on the market. Thomas Adams first manufactured MCGs with a natural latex-based and issued the first patent for the chewing machine to render chicle kneaded, and smooth but modern chewing gum soft enconsist of synthetic resins. There is a monographin European Pharmacopeia (EP) that defines MCG but the term "chewing gum" was first listed in guidelines as a pharmaceutical dosage form in 1991 and approved by the commission of European communities[4,]

Advantantages of medicated chewing gums

1. Increased rate of effectiveness rather than another or al dosage form.
2. Use for both systemic and local action.
3. Does not require water to swallow, hence can be taken anywhere.
4. Avoid first-pass metabolism and thus increases the bio availability of the drug.
5. Fast onset of action due to rapid release of the drug.
6. High accept an ceby children and teenagers.
7. Good stability against light, oxygen, and moisture.
8. Convenient -promoting higher compliance .
9. Discreet less stigmatization.
10. Excellent for acute medication .[5]

Disadvantages of medicated chewing gums

1. Getting choked by swallowing gum in under-aged children.
2. Risk of over dose.
3. Prolong chewing on gum may result in pain in facial muscles.
4. It may adhere to enamel dentures and fillers.
5. May causes to mach irritation and gastric ulcers.
6. Different release profiles because of chewing style differences.
7. Teeth decay through being coated with sugar.
8. Highly acceptable by children.
9. Pleasant teste .
10. Candidacies and caries.[6]

1.3 METHOD FORMULATIN CHEWINGUM

1.3. Fusion method

The first step of a typical process for manufacturing chewing gum is to melt and soften the gum base at about 60°C and place it in a very kettle mixer, within which blades soften the bottom, then other ingredients like sugar, glycerine, sweeteners, taste-masking agent are added to the softened base, lately, the flavouring agent is added within the mixing procedure at 40°C, then cooling and rolling steps would be done, and also the rolled chewing gum would then delve pieces of desired shapes and sizes. A coating agent should be sprayed to makean identical surface to form a coated gum tablet.

The second form of this method is somehow different: the first step of preparation is to line up a mixer (the mixer may well be a sigma blade or other varieties of mixers), if a sugar-containing gum is required, the primary step is to feature syrup to the mixer, so finely granulated sugar is added gradually. Sugar, employed in this step, can be powdered sucrose, dextrose, fructose, syrup solids, or a mixture of them. Glycerine is the most preferred plasticizer used. Other components specified could be added to the matrix according to required characteristics, such as fillers, colorants, and flavouring agents. But it is recommended that flavors be added to the matrix at the end of procedures when the gum base is totally and completely homogenized because most flavors are relatively volatile. The proportions of components in the matrix are variable between sources and depend on desired characteristics. But powdered sugar has approximately the most proportion.[4,7]

The mechanical forces of the mixer, that is, compressive and shear, and warmth can ease the softening process. When no heat is applied, a better power is demanded. the blending process continues until a standardized mass is created. the blending process should last about 8min. otherwise blending ingredients is to feature sugar gradually till the top of adding other components. After matrix preparation and completely mixing, the commercially prepared particles of gum base are added to the chamber all at once. But it is believed that these particles should have been heated and mixed before adding all othering redients to the mass of the gum base. In thisstage, mixing willcontinuefor10-20min.[7]

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Cooling, grinding, and tableting method

One other method to supply a chewing gum with the specified taste, color, and therefore the flavors is to combine the gum base with favorable and suitable sweeteners, corn syrups, starches, flavoring agents, and colorants, then refrigerate and funky it with a freezer apparatus or by contracting with a coolant like CO2 to a temperature below −15°C which is therefore crushed and pulverized with acutter or grinding apparatus to get minute particles then these finely ground particles are heated to a temperature which makes them adhere to every other and form a slick and uniform bulk with consistent texture and low relative density. If the fragments are such they are not self-adhesion and could be applied manually or mechanically before they're warmed to the conventional temperature to there by promote self-adhesion. The cooling and grinding steps can be combined by cooling the grinding apparatus. After the grinding step, we can let the coolant (if used) evaporate and disappear from our desired composition. The minute particles may be coated with edible substances or premixed with powdery materials.[8]

Direct compression

A new technology to create a chewing gum tablet is direct compression and tableting at the high-speed standard machine, but as explained during a patent, this manner of forming chewing gum tablets provides a quickly is sociable chewing gum, but after some seconds of chewing, particles adhere together to make an identical and homogenous mass. during this method; we'd like a granulating agent, preferably sorbitol, which might also act as a sweetener. A lubricant like magnesium stearate, talc, octadecanoic acid, hydrogenated vegetable oils, and sodium stearyl fumarate is added to the formulation before tableting. The primary step of this method is dry mixing of gum base, granulating agent, and aminimum of one processing material then adding an energetic ingredient, sweeteners, and other needeing redients to the formulation within the free-flowing wine sort of materials then directly compressing the chewing gum tablets.[9]

II. LITERATUREREVIEW

1. **Durga Devi. et.al.(2021),:-**The production of chewinggum in the global chewinggum market is rapidly increasing from USD 25 billion to an estimated USD 37 billion by the year 2023. The application of chewing gum in the drug delivery system has increased compared to pharmaceutical pre-dosage form. However, gum bases are Split out after chewing which generates non-biodegradable waste causing harmful effects to the environment as well as living organisms. The review confers adequate information to increase the scale of production of biodegradable chewing gum for delivering bioactive compounds as well as zero-waste technology which sustainably reduces environmental pollution.
2. **Indumathi .et.al.(2020),:-** Chewing gums are mobile drug delivery systems. The extract of the herbal medicines may be incorporated into the chewing gum and may be utilized in the treatment of mouth ulcers. it was concluded that chewing gum is a wonderful drug delivery system for self-medication. Natural gum base is economical, safe, and environmentally utilized in the treatment of assorted mouth diseases.
3. **Azra Shake. et.al.(2017),:-** An attempt was made to formulate new chewing gum for Dolasetron. The new drug delivery system was obtained, at room temperature with conventional pharmaceutical equipment. The resulting chewinggum comprises a gumcore combined with fillers, antioxidants, coloring agents, and plasticizers, which provide a smooth appearance and flexibility during storage and chewing. Drug release from a dosage form is the critical step in drug absorption and bioavailability, thus an experimental work has been designed to evaluate the efficiency of this kind of therapeutic system by verifying its capability to release the drug dose and by assessing the delivery of dolasetron for bypassing the hepatic first-pass effect. In the present study,an attempt has been made to formulate the chewinggum of Dolasetron. From this study, we can conclude that the medicated chewing formulation can be a better choicein the coming years which provides several benefits and also benefits commercially.
4. **Manasi paradkan. et. al(2016),:-** Medicated chewing gum (MCG) of Domperidone Maleate (DM) was developed by direct compression method to achieve quick onset of action and improve patient compliance. MCG containing DM was prepared by screening different concentrations of sweeteners, flavoring agents, softening agents, lubricants, and anti-adherents by changing one variable at a time.

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Performance evaluation was carried out by evaluating size, shape, thickness, taste, scanning electron microscopy, texture analysis, and in vivo drug release study. The statistical analysis showed significant improvement in organoleptic properties such as chewable mass, product taste, product consistency, product softness, total flavor lasting time, and pharmaceutical properties. The developed formulation of medicated chewing gum can be a better alternative to mouth dissolving and conventional tablet formulation. It may be proved as a promising approach to improve bioavailability as well as improve patient compliance.

5. **Rahul Shetty. et.al (2016),:**-An attempt was made to formulate medicated chewing gum to prevent motion sickness using natural gum base for faster onset of action and easy administration, anywhere and anytime, without access to water. Chewing gum could be a soft, cohesive substance designed to be chewed without being swallowed. Modern chewing gum consists of gumbase, sweeteners, softeners/ plasticizers, flavours, colours, and a tough or powdered polyol coating. Its texture is paying homage to rubber because of the physical-chemical properties of its polymer, plasticizer, and resin components, which contribute to its elastic-plastic, sticky, chewy characteristics.

6. **Ritesh Kumar. et.al.(2014),:-** Explained that unlike chewable tablets medicated gums aren't alleged to be swallowed and should be off from the location of application without resorting to invasive means, and medicated chewing gum MCG could be a solid, single-dose preparation. Since it **is** taken any where, a chewing gum formulation is a wonderful choice for acute medication. the benefits for youngsters and for patients who find swallowing tablets difficult are obvious. The 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 the buccalmucosa.

7. **PrashantP.Pagare.et.al.(2012),:-**
Chewinggum is one of the very popular oral confectionery ducts. It's a potentially useful means of administering drugs either locally or systematically via, oral fissure. The medicated chewing gum has through the recent years gained increasing acceptance as a drug delivery system. It offers various advantages over conventional drug delivery systems. More over-medicated chewing gums require active and continuous masticatory activities for activation and continuation of drug release. An In-vitro apparatus was specially designed and constructed for releasetesting of medicated chewinggums. Medicated chewing gums are excellent mobile drug delivery systems for self-medication.Itoffers various advantages over conventional drug delivery systems.

8. **VipulP.Patel.et.al.(2011),:-**Severaling redients are now in corporate in medicated chewing gum, ex. Fluoride for prophylaxis of dental caries, chlorhexidine as a 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 the prevention of caries, xero stomia alleviation, and vitamin/mineral supplementation are currently available.[10]

DRUG PROFILE:

- **Structural formula:**

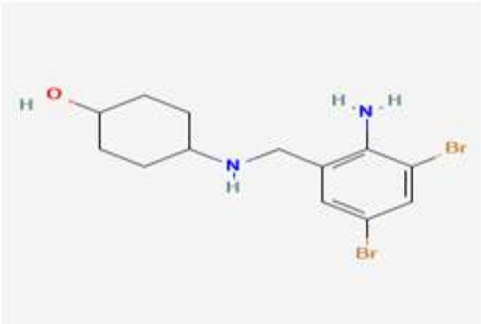


Figure1 Structural Formula of Ambroxol HCl

- **Synonym:** rac-cis-Ambroxol
- **Empirical formula:** $C_{13}H_{18}Br_2N_2O$
- **Chemicalname:**4-((2-amino-3,5-dibromobenzyl)amino)cyclohexane-1-ol
- **Boilingpoint:**468.6ºCat760mmHg
- **Meltingpoint:**235-240ºC[17]

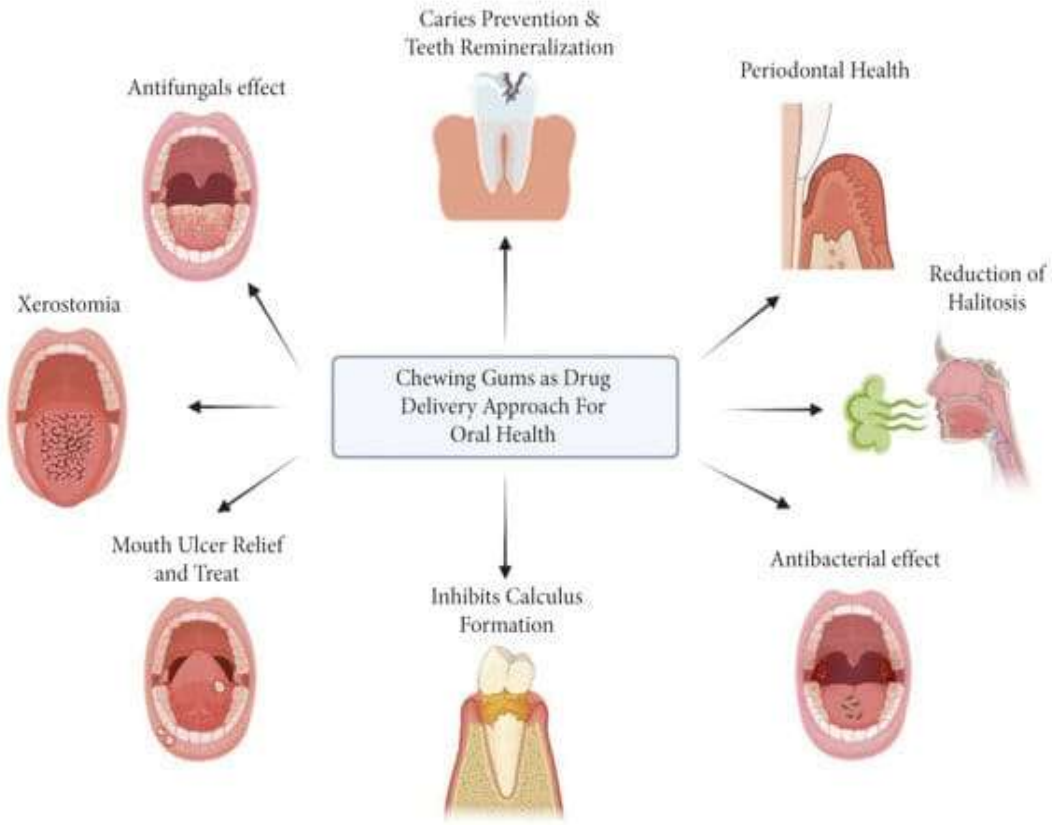
- **Mechanism of action:** Ambroxol HCL is a clinically proven systemically active mucolytic

International Journal of Pharmaceutical Research and Applications
Volume 8, Issue 6 Nov-Dec 2023, pp: 1294-1302 www.ijprajournal.com ISSN: 2249-7781

agent. When administered orally onset of action occurs after about 30 minutes. The breakdown of acid mucopolysaccharide fiber makes the sputum thinner and less viscous and therefore more easily removed by coughing. Although sputum volume eventually decreases, its viscosity remain slow for as long as treatment is maintained.[18]

Gum For Cough.

- **Ambroxol HCL Indications:** All forms of tracheobronch it is, emphysema with bronch it is pneumoconios is, chronicinflammatory pulmonary conditions, bronchiectas is, bronchitis with bronchospasm asthma. During acute exacerbations of bronchitis, it should be given with the appropriate antibiotic.
- **Ambroxol HCL Contraindications:** There are no absolute contraindications but in patients with gastric ulceration relative caution should be observed.
- **Ambroxol HCL Side effects**: Occasional gastrointestinal side effects may occur but these are normally mild.
- **Precautions:** It is advisable to avoid use during the first trimester of pregnancy.[11]



III. DISCUSSION

3.1 PROBLEMS ASSOCIATED WITH THE MANUFACTURING OF CHEWINGGUM:

Capping, lamination, picking, and sticking are the most common processing problems. 2.Heating and melting can make controlling the accuracy and uniformity of the drug difficult.3.It is hard to provide sanitary conditions to make MCGs. In the second method, the moisture content of chewing gum may cause the gum to jamto the blades and punches of apparatus, screens, surfaces, and chamber's wall. In the second method caking and balling of the gum prevent the formation of gum fragments. Forming alow-calorie chewing gum has resulted ingum with hard chew, poor texture, and bad taste or off-taste. Sugar spots or lumps may appear in the final texture and cause an undesired feeling. Some ingredients and active agents can irritate the mucosa. High temperature to facilitate the mixture of gum base, leads to spoiling other

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ingredient. Water eliminate in from final formulation require advaced technique to avoid the had ness of chewing gum .[12]

3.2 PROBLEMSOVERCOMEDURINGFORMULATION:

- We used chewing gum for drug delivery because of its acceptance in children, its bioavailability is also good, it has a pleasant taste, and it is easily available
- Initially, we took 7gm of chewing gum mass, the nadded 8mg of Ambroxol HCL to the chewing gummass, and the remaining 2mg was added in the liquid form by making acavity and molding it.
- Chewinggum is generally categorized as food but the addition of drugs makes it medicated so it is categorized in medicatication.
- We overcome the leakage of the drug by increasing the thickness of chewing gum thus making it tough.
- We can't mask the taste of the drug but by increasing the amount of sucrose during formulation, we can minimize the bitterness of the drug.

3.3 STABILITY:

Chewing gum is a very stable product due to its low moisture content and less reactive nature than that other oral ingredients. A major challenge in the production of chewing gum is its shelf life, storage conditions, and effect of some ingredients that impress stability. Water content can lead to the growth of micro organisms and chemical degradation, but water canbe bound to other compounds, so that is not noticeably available to active agents, even if little water exists in the chewing gum is determined to annihilate and dangerous for other components, no water can be employed in the manufacturing method. To avoid oxidation of the drug, antioxidants are needed but due to the low content of water, the presence of preservatives is not essential.[4,14]

Holding water content with no significant change at low or high concentrations of moisture within the atmosphere needs a serious amount of gum base and xylitol as a bulking agent. Such made chewing gums are stable in extreme conditions and are capable of adding more desired ingredients and active agents. No stiffening, compacting, or softening is observed in terms of moisture stability in these forms of gums. Xylitol would also enhance storage stability within the gum; it means in low or high humid conditions the gum's water content remains at its level and therefore the gum flexibility, elasticity, splitting, and softness don't encounter major changes. The effect of xylitolon the crystalline structure and its water-binding properties are to blame for these changes.[14]

Generally, the stability of the active substance is good because chewing gum holding drug protects it from oxygen, light, and humidity. The high temperature for some heat-sensitive componentst of acilitate mixing can be avoided by increasing other powers, instead. Undesired interactions between different components can be prevented by encapsulation or coating some ingredients with suitable substances so that less contact between compounds occurs. One other important parameter involved is appropriate packaging and storage of gum to prevent water and moisture penetration and light exposure. The costly packaging and wrapping can be eliminated by spotting the above notes. Finally, the freshness and stability of gum would remain for along period and the problem of staling, brittleness, and/or growth of micro organisms can be greatly reduced.[13]

a. SAFETY ASPECTS:

Generally,nowadaysitisperfectlysafetochewchewinggum.Previously,hardchewinggumhascaused broken teeth. Extensive chewing for a long period may cause painful jaws muscle, and extensive use of sugar alcohol containing chewing gum may cause diarrhea. Long-term frequently chewing of gum cause increased release of mercury vapors from dental amalgam fillings. However, medicated chewing gum does not normally require extensive chewing or a consumption to great extent. Flavors, colors, etc. may cause allergic reactions. Overdosing by the use of chewing gum is unlikely because a large amount of gum has to be chewed in a short period to achieve this. Swallowing pieces of medicated chewing gum will only cause the minor release of the drug because the drug can only be released from the gum base by active chewing. As a general rule, medicated chewing gum (like other medicines) should be kept out of reach of children, if required; drug delivery may be promptly terminated by removal of the gum .[14]

b. FUTURE TRENDS:

The future of chewing gum will reveal all of the scientists' efforts for the event of chewing

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Volume 8, Issue 6 Nov-Dec 2023, pp: 1294-1302 www.ijprajournal.com ISSN: 2249-7781

gum as acon temporary drug delivery system and therefore the progress of chewinggum production technology. In the future, other attempts are seen to formulate more drugs using chewing gum as a drug delivery system. Treatment of fungal diseases, prevention of caries and other dental health issues, smoking cessation, etc., are common health works of MCGs. But remineralization of teeth, cold relief, energy enhancement, and anti-nausea so many new advantages of this novel drug delivery system are visiting play a very important role infuture studies. It takes time for chewing gum to induce acceptance by people as a drug delivery system, but we hope that MCG finds its real place in industry and market and among patients soon, through its numerous advantages. Long-lasting flavored, filled gums, timed-release, and other new MCGs formulated for diseases that previous delivery systems are used for, are trendy products to be seen within the future as a replacement reason ably chewing gum that's made biodegradable and may be dissolved in around 1 month. We predict a brighter future for MCG as a unique drug delivery system than previous oral systems.[15.16]

FIGURE NO. 4

FIGURE NO.5

FIGURE NO.6

IV. CONCLUSION

Thus it can be concluded that the chewing gum can be used as a carrier for vast categories of drug were extended realease and the local action is described . Chewimg gum can be used without water at any time medicated chewing gum can produce both local effects as well as systemic effects in the oral cavity they can be used for the purpose of taste masking of certain drugs . Chewing gum not only of offerce clinical benefits but also is an atrractive distinct and effect efficient drug delivery system . Clinical trais have conform the benefits that can be gainted by exploting the effects the chewing gum is of delivery and apportunitis for buccal cavity absorption and local effects . The current manuscript present many of the petented applicatin ued in the field of chewing gum. Managment of fungal infection prevention of carries, smoking cessation ,decaying gums .

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Volume 8, Issue 6 Nov-Dec 2023, pp: 1294-1302 www.ijprajournal.com ISSN: 2249-7781

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