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BRIEF OVERVIEW: THE FUNDAMENTALS OF FORMULATING AND EVALUATING CHEWABLE TABLETS WITH A BITTER MASKED TEST

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ABSTRACT

Tablets that can be eaten between the teeth must be broken before consumption. These tablets are provided to individuals who detest swallowing and to youngsters who have trouble swallowing. Whether or not they are really chewed, typically chewable tablets dissolve smoothly, taste good, and leave no bitter or off-putting aftertaste. Patients who need easy-to-swallow dosage forms, like chewable pills, the most include elderly and paediatric patients, as well as patients travelling who might not have ready access to water. The gum core of a chewable tablet, which may or may not be coated, makes up its composition. Insoluble gum base, fillers, waxes, antioxidants, sweeteners, and flavourings make up the core. Depending on the base utilised and its characteristics, the percentage of gum base ranges from 30 to 60%. To make it more appetising, a flavouring agent is added. The composition of chewable pills takes into account a number of variables. Organoleptic qualities of the active medicinal ingredients are the main focus here, but other formulation parameters like flow, lubrication, disintegration, organoleptic features, compressibility, compatibility, and stability also play a vital role. To create a formula and process combination that yields a product with good organoleptic qualities, a formulator may employ one or more methods. The flow, compressibility, and stability properties of this substance must be satisfactory.

KEYWORDS: Gum core, compressibility, chewable tablet, antioxidant, etc.

INTRODUCTION

Tablets that must be broken and eaten in between the teeth before consumption. Children who have trouble swallowing and adults who detest swallowing are given these tablets. Chewable tablets often have a smooth texture upon disintegration, are pleasant tasting, and leave no bitter or disagreeable taste. These tablets are meant to disintegrate smoothly in the mouth at a reasonable rate with or without actual chewing. In order to create a strong solid dosage form, developing a tablet formulation successfully requires the careful selection of ingredients. To achieve satisfactory manufacturing performance, the right excipient must be chosen to carry out a particular function in a tablet formulation, such as disintegration or lubrication. To cover up the unpleasant flavours and make paediatric dosing easier, chewable tablet formulations frequently contain sweeteners, both manufactured and naturally occurring. They should ideally dissolve in the mouth when chewed, releasing their components as they do so. This reduces the amount of time needed for tablet disintegration before stomach absorption. When the active ingredient is meant to work locally as opposed to systemically, chewable tablets are frequently used. A palatable chewable tablet is one that can be consumed with little to no water after being chewed. Wet granulation or direct compression are typically used in the production of chewable tablets. Depending on the base utilised and its characteristics, the percentage of gum base ranges from 30 to 60%. It has a flavouring ingredient to make it more appetising. To ensure patient acceptance and compliance, taste-masking procedures are used to cover up or eliminate the bitter or unpleasant taste of active medicinal ingredients/drugs. For patient populations including paediatrics and geriatrics, oral administration of bitter or unpleasant-tasting medications is sometimes the main hurdle. The mechanics of taste-masking techniques frequently rely on two main strategies: the first is to mask the unpleasant taste by adding sweets, flavours, and effervescent agents; the second is to prevent the contact of bitter or unpleasant medications with taste buds. By utilising cutting-edge methods and techniques, like hot-melt extrusion and microencapsulation, major advancements in taste-masking have been realised in recent years. The industrial methods and platforms utilised for taste-masking in oral dosage forms are described below along with their current status.

Considerations for flavor-masked formulations

For flavor-masked formulations, the dissolution profile and taste profile both contribute to the acceptability standards. Nevertheless, depending on the dose strength and organoleptic response to the API, each therapeutic product will have variable release profile needs to

satisfy an acceptable amount of taste-masking. The taste-masked dose form should, in ideal circumstances, delay release of the bad-tasting medication until the API has left the mouth and then permit immediate release after the dosage has been consumed. While electronic tongue technology is developing, taste panels continue to be the preferred tool for testing the effectiveness of taste masking. Depending on the drug's solubility and additional additives like flavours and sweeteners, patients may be able to tolerate varying degrees of release in the mouth for various APIs. Depending on the drug's solubility and other formulation components such flavours and sweeteners, patients may be able to tolerate varying degrees of release in the mouth for various APIs. Some regulatory bodies have advised against using the formulation's ability to taste as a defence against people mistaking it for candy. Taste profiles should strive for a taste that is neutral or widely regarded as acceptable. the mouth's flavour. The objective of taste-mask coating, particularly in the case of paediatric dosage forms, is to achieve robust functionality with the least amount of weight gain possible. However, the characteristics of the substrate will affect effective weight growth.

Basic Formulation Element

Chewable tablet formulation involves a number of variables. The main formulation factors, which apply to both chewable and normal tablets, are flow, lubrication, disintegration, organoleptic qualities, compressibility, compatibility, and stability. However, in this case, the organoleptic properties of the active drug components are of key significance. A formulator may employ one or more strategies to come up with a formula and process combination that yields a product with favourable organoleptic qualities. An adequate level of flow, compressibility, and stability must be present in such a substance.

Fragrance and taste

The physiological definition of taste is a sensory reaction brought on by the chemical activation of taste buds on the tongue. Salinity, sourness, sweetness, and bitterness are the four primary flavours. Objects that can ionise in a solution are what give foods their salty or sour flavours. Although they might not be able to ionise in an aqueous solution, many organic therapeutic substances cause a bitter response. A majority of saccharides, disaccharides, some aldehydes, and a small number of alcohols have a sweet taste. Tasteless refers to a substance that is unable to stimulate the senses. A distinct combination of taste and smell is referred to as a flavour in most contexts. In contrast to honey, which has both a sweet taste and a flavour, sugar, for instance, only has a sweet taste.

Mouth-feel

This word refers to the kind of taste or touch that a tablet makes when it is chewed in the mouth. Therefore, it has nothing to do with chemically stimulating taste or olfactory receptors. The entire impact in the mouth is crucial for a formulation to be successful. In general, a smooth texture with a calming and cooling sensation is favoured versus a gritty or sticky texture (for example, calcium carbonates).

Aromas

Aromas are typically described as pleasant odours. For instance, a properly designed chewable tablet with orange flavour should have the distinctive sweet-sour flavour and aroma of a real orange.

Subsequent Effects

The most frequent side effect of several substances is aftertaste. For instance, some irons have a "rusty" aftertaste, while sucrose in large doses often has a bitter aftertaste. Another frequent side effect is a section of the tongue and mouth's surface feeling numb. This family of medications typically includes bitter antihistamines like promethazine hydrochloride and pyribenzamine hydrochloride.

The Demand for Chewable Tablet Development: Due to patients' poor compliance and acceptance of current delivery regimens, the small market size for pharmaceutical companies and drug uses, as well as the high cost of illness management, the demand for non-invasive delivery systems continues.

1. Efficacy-Related Factors

One of the main claims made for these formulations is increased bioavailability and quicker onset of effect. Pre-gastric absorption can be quite advantageous for medications that undergo a lot of hepatic metabolism since it prevents first pass metabolism. Additionally, for medications that significantly increase the production of hazardous metabolites through first-pass liver metabolism and stomach metabolism.

2. Factors That influence Manufacturing and Marketing

Regardless of their size, pharmaceutical firms must create innovative drug delivery technologies and use them in product development to thrive. It is typical for pharmaceutical companies to create a certain drug entity in a new and enhanced dosage form as a drug

approaches the end of its patent life. A novel dosage form enables a firm to give its patient population a more practical dosage form while extending market exclusivity, distinctive product differentiation, value-added product line expansion, and patent protection. This targets patient populations that are underserved and undertreated while also increasing revenue.

3. The patient's circumstances

About one-third of patients require immediate therapeutic effects from drugs, which results in poor adherence to conventional medication therapy and lower overall therapy. There has been a development of a novel dosage form called instant release tablets, which combines the benefits of convenience and ease of administration. These tablets are made to release the medications more quickly. Chewable dose forms are especially useful for appropriate for people who find it uncomfortable to swallow regular tablets and capsules with a glass of water for one reason or another. Patients who are very old and may not be able to swallow an antidepressant daily.

4. Evaluation of the Issues with Formulation

Whenever possible and reasonable, getting a complete profile of the active medication is the first step in the manufacture of a chewable tablet. As the drug usually determines the choice of fillers, transporters, sweeteners, flavour compounds, and other product modifiers, this usually results in the formulation of a stable and quality product that is most effective. The optimal medication profile would include details on the following.

Physical Features

- Colour \odour
- Taste, lingering flavour, and mouthfeel
- Physical forms include liquid, powder, amorphous solids, crystals, and more.
  Melted ice level
- Polymorphism
- Content of moisture aqueous solubility
- Stability of active drugs
- Compressibility

Chemical Features

- Chemical classification and structure
- Major responses
- Important incompatible substances
- Drug dosage

This active drug profile would eliminate flavourings and excipients that would not be compatible with the drug, allowing for the use of those that would physically, chemically, and organoleptically complement the drug the best. Excipients and other product modifications should be chosen while considering both their cost and functionality. With customers worried about calorie consumption and dental caries, using low-caloric and non-sugar excipients may offer a marketing advantage.

Taste Enhancing

Flavor masking is the term used to describe the elimination of an unwanted taste. Taste masking chemicals, particular flavours, and sweeteners can all be used to disguise certain tastes. Sweeteners are necessary to finish the experience and give the product a pleasing flavour. This is a key limiting element in the development of oral dose forms with disagreeable tastes. The two main solutions to this issue are flavour masking and processing techniques. Flavor, sweetener, fat, and acid additions are frequently used to disguise flavours.

Approaches for Masking Taste

Before formulation, there were certain typical issues like terrible mouthfeel and taste. The desired product should have a flavour and sweetener that are appropriate, a decent tongue feel, and good compressibility. It should also prevent or reduce stimulation of the taste buds. These issues are resolved using the subsequent methods:

- Wet granulation coating
- Microencapsulation
- solid agglomerations
- Techniques for Adsorbate Formulation (Solvent method)
- Exchange of Ions
- Congealing and coating with a spray
- synthesis of various salts or derivatives
- Utilization of protein hydrolysates and amino acids

- Integrated complexes
- Complex molecules

Polymer coating

The simplest technique is direct coating, which uses a substance that is insoluble in the mouth to create a physical barrier around the drug particles. Lipids, sweeteners, and hydrophilic or hydrophobic polymers can all be employed alone or in combination to create a single layer of coating or many layers. With polymer coat levels ranging from 10% to 40%, depending on the bitterness of the medicine, methacrylic acid and methacrylic ester copolymers (Eudragit E-100, RL 30D, RS 30D, L30D-55, and NE 30D) have been successfully employed for taste-masking.[9] The method of choice is frequently a fluid bed. Recently, alternative methods have included coating medication particles with molten lipids, such as glyceryl palmitostearate (Precirol® ATO-5, Gattefosse, France) and glycerol behenate (Compritol® 888-ATO, Gattefosse, France).

The second option entails depositing an active substance in layers upon beginning seeds that are inert, like sugar spheres or celpheres. For the bitter medicine to cling to the inert substrate, it is dissolved or dispersed in an aqueous or non-aqueous solvent with a binder. Hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), povidone, Eudragit E-100, and carboxymethyl cellulose are a few of the binders that are frequently utilised. After that, a taste-masking polymer is applied to the drug-layered beads to prevent the drugs from dissolving in the mouth. Eudragit E-100, ethylcellulose, HPMC, HPC, polyvinyl alcohol, and polyvinyl acetate are a few polymers that are used to conceal tastes. 7 The final dose form, such as a capsule or a crushed tablet, can then contain the taste-masked coated beads.

GENERAL INGREDIENTS INCLUDED IN CHEWABLE TABLET FORMULA

The substances that serve as the foundation for the manufacture of chewable tablets, however, require special attention. Taste and, to a lesser extent, appearance will be the main determinants of acceptability in the composition of chewable pills. Therefore, it is crucial to choose and use components that have an impact on these attributes wisely. The end product must be as pure, safe, effective, and stable as any other; the formulator must, however, be mindful of various pharmacological and biological factors in addition to these features.

Chewable tablets can be processed using the same wet granulation, dry granulation, direct compression, and direct compaction methods as other types of tablets.

Sweetners

1. Dextrose:- The sugar that results from completely hydrolyzing starch is called dextrose. It comes in anhydrous (though hygroscopic by nature) and monohydrated forms, and its sweetness level is roughly 70% that of sucrose.

2. Mannitol:- A white, crystalline polyol called mannitol is half as sweet as sucrose. Due to its negative heat of solution, it is freely soluble in water and when chewed or dissolved in the mouth, it provides a light cooling feeling. Mannitol has become the preferred excipient for formulations of chewable tablets as a result of this and its unusually smooth consistency.

3. Lactose:- Whey, a byproduct of the cheese-making process, is the source of the monosaccharide lactose. Despite being largely recognised as the medicinal excipient that is utilised the most everywhere. Due to its incredibly low sweetness level (15% sucrose), its applicability to chewable pills is minimal at best. Due to lactose's blandness, this deficit necessitates the addition of an artificial sweetener with suitable strength. Regular pharmaceutical grades (hydrous fine powders) are offered for wet granulation applications. Lactose is an anhydrous powder with good flow and compressibility properties that can be compressed directly.

4. Flavouring agents:- Taste is almost certainly the most significant factor in the evaluation of chewable tablets from the standpoint of consumer acceptance. Taste is a fusion of the sensations of sweetness, flavour, and mouth-feel. The temperature of the soluble component's solution, the combination's smoothness when chewed, and the tablet's hardness all have an impact on how the food feels in the mouth. The active component and main excipients are directly and largely responsible for these factors. Any flavour requires a background of sweetness, at the proper level.

Manufacturing

Manufacturing for chewable tablets include achieving the right level of tablet hardness, maintaining the right moisture content, and properly incorporating the colouring ingredient. Once the parameters have been defined throughout development, the manufacturer in the department is routinely responsible for all of these. In order to guarantee the accuracy of the specifications, the process development and scale-up considerations should be carefully studied. The blending process involves adding coloured powder to white granules if the

colour is added as a lake for direct compression mix. As a result, the coloured powder will cover the white granules uniformly. However, the granules release new white material to the surface during compression, creating "speckling"—white patches on a coloured backdrop.

GENERAL TECHNIQUES FOR PROCESSING CHEWABLE TABLETS

The following techniques were applied to create the chewable tablets.

1. Dry granulation or non-aqueous granulation.
2. Wet granulation or aqueous granulation.
3. Direct compression.

Granulation

Granules are formed when smaller, single-particle entities known as primary powder particles are forced to stick together during the granulation process. Granules used in pharmaceuticals range in size from 0.2 to 4.0 mm. Powder flow and compressibility can be improved with granulation, and the segregation of the blend's component parts can be avoided. Two techniques are mainly used in granulation.

1. Dry granulation

It is a novel technique for producing granules in a semi-automatic fashion. Any pharmaceutical medication with a solid dose form can be used with this strategy. Existing solid dosage form development and manufacturing technologies are replaced by the dry granulation method, which allows for quicker development and better quality. The powder combination is compacted using this method without the aid of heat or solvent. There are two approaches to dry granulation. Slugging, which involves recompressing the powder and milling the resultant tablet to produce the granules, is the more popular method.

2. Wet granulation

The most popular granulation technique is wet granulation. Wet massing of a powder mixture with a granulating liquid, wet sizing, and drying are the steps in this procedure. The granulating liquid comprises a solvent that must be non-toxic and volatile so that it may be eliminated by drying. Water, ethanol, and isopropyl alcohol are common liquids. The wet mass is driven through a screen in the conventional wet granulation process to create wet granules that are then dried.

Direct Compressed

The most popular option is direct compression because it offers the quickest, most efficient, and simple method of creating tablets. When a number of substances may be blended, this technique is typically used. Since it does not require soaking or drying, it is better suited for APIs that are sensitive to heat and moisture. It also increases the stability of the active ingredient by minimising negative (bad) effects. This procedure involves mixing the API with the excipients and lubricant before compressing the mixture to make the product simple to handle.

PARAMETERS FOR EVALUATION OF CHEWABLE TABLET

When creating chewable pills, a range of evaluation criteria must be considered. These are listed below.

1. In-process organoleptic assessment.

This assessment happens at numerous points during the creation of a chewable tablet. These are listed below.

2. Analysis of the drug.

It entails characterising and evaluating the substance either in absolute terms or in comparison to a recognised reference standard.

3. Evaluation of the unflavoured base formulation.

Entails comparing various vehicles, the percentage of vehicles, or other formulation factors when the drug is coated.

4. Comparison of several flavoured formulations.

It is required for the evaluation of the baseline flavour formulation.

5. Evaluation of a coated drug.

This process compares the coated drug to the pure drug and takes different coating treatments into account.

Chemical Analysis

1. Drug content analysis.
2. Uniformity of dosage.
3. Evaluation in vivo and in vitro.

Physical Assessment

1. The appearance of the tablet.
2. Hardness.

3. Dissolution.
4. Disintegration.
5. Friability.

CONCLUSION

In conclusion, there are numerous taste-masking technologies employed in the pharmaceutical sector today, and new ones are continually being explored and created. The chosen technology is mostly determined by the physical and chemical characteristics of the medicinal component and the intended final dose form. The pharmaceutical industry has been able to offer commercial products with improved patient acceptability and compliance, especially with paediatric and geriatric populations; along with increased convenience for patients on the go, thanks to advancements in taste-masking technologies over the past few years. To expand their product lines for oral dosage forms, more businesses are relying on taste-masking expertise.

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