1. Introduction

Chewable tablets are a medicinal dosage form designed to be chewed before swallowing. Chewable tablets are gaining popularity because of their ease of use and practicality for patients, especially children, and adults, who have difficulty swallowing regular tablets or capsules. One interesting approach in the formulation of chewable tablets is to use natural extracts as active ingredients. Extracts of natural materials are concentrated forms of natural materials produced through an extraction process using certain solvents. This natural substance is often used in pharmaceutical products because it has significant therapeutic potential and can provide the desired pharmacological effect. 1-3

Formulation of chewable tablets from extracts of natural ingredients requires special attention in designing preparations that maintain the quality and stability of the active ingredients. The extract must have the desired pharmacological effect and be proven safe to use. This study aimed to carry out a systematic review in order to explore formulations of chewable tablets made from natural ingredients. The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the formulation and evaluation of chewable tablets from natural extracts. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations. Formulation of chewable tablets from extracts of natural ingredients is an interesting approach in the development of pharmaceutical preparations. Through a selection of appropriate extracts, careful evaluation of stability, and attention to taste and aroma, these chewable tablets can provide significant benefits to patients. However, it is important to carry out careful research and testing to ensure the safety, effectiveness, and quality of these products before they are used in clinical practice.
to produce tablets that are easy to chew and taste good on the tongue. Chewable tablets should have a pleasant taste and aroma to improve patient compliance to consume it. Appropriate natural flavoring agents can be used to provide a pleasant taste without compromising the quality of natural ingredient extracts. In addition to considering stability and formulation, the safety and effectiveness of chewable tablets from natural extracts must also be evaluated through clinical trials and strict supervision. This study aimed to carry out a systematic review in order to explore formulations of chewable tablets made from natural ingredients.

2. Methods

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the formulation and evaluation of chewable tablets from natural extracts. The search was performed using the terms: (1) “formulation” OR “evaluation” OR “chewable tablets” OR “extract” AND (2) “formulation”. The literature is limited to preclinical studies and published in English. The literature selection criteria are articles published in the form of original articles, an experimental study about formulation and evaluation of chewable tablets from natural extracts, the control group only received liquid without therapeutic effect or no treatment, studies were conducted in a timeframe from 2000-2023, and the main outcome was formulation and evaluation of chewable tablets from natural extracts. Meanwhile, the exclusion criteria were animal models that were not related to the formulation and evaluation of chewable tablets from natural extracts, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

Figure 1. Research PRISMA diagram.
3. Results and Discussion

Evaluation of natural ingredients in chewable tablet preparations

Evaluation of the stability of extracts of natural ingredients in chewable tablets is very important to ensure the integrity and effectiveness of the active ingredients. Several factors to consider in evaluating stability include temperature, humidity, and storage time. Storage temperature can affect the stability of natural product extracts. Some extracts can become unstable or degrade at certain temperatures. Therefore, it is important to determine the proper storage temperature to maintain the integrity of the active ingredients in chewable tablets. Usually, storage temperatures in the 20-25°C range are most commonly used, but some extracts may require lower or higher temperatures.8,9

Moisture is a critical factor in evaluating the stability of natural product extracts. High humidity levels can cause chemical changes, absorption of water, or growth of microorganisms which can reduce the stability of the active ingredients. Therefore, chewable tablets should be stored in an airtight container capable of protecting against excess humidity. Storage time is an important factor in stability evaluation. Chewable tablets should be tested periodically during the storage period to monitor physical, chemical, and pharmacological changes. This helps in determining the proper shelf life for the product and ensures that the active ingredients remain stable for the desired shelf life.10

Chewable tablet formulation technique

In the formulation of chewable tablets, it is important to consider the taste, texture, and stability of the tablet in order to create a product that is easy to chew and tastes good on the tongue. Excipients are used to provide the required volume and density in chewable tablets. Excipients must be carefully selected to ensure compatibility with the active ingredients and the ability to form solid tablets. Examples of commonly used fillers are lactose, sorbitol, mannitol, and microcrystalline cellulose. Lactose is a milk sugar that is often used as a filler in chewable tablets. It gives density and volume to the tablet. However, it should be noted that lactose can be a problem for individuals who are lactose intolerant. Sorbitol is a natural sweetener that is often used as a filler and sweetener in chewable tablets. It imparts a sweet taste to tablets and has good binding properties. Sorbitol can also provide a mild laxative effect when taken in large amounts. Mannitol is a sugar alcohol used as a filler and sweetener in chewable tablets. It has a pleasant sweet taste and imparts good hardness to the tablets. Mannitol is also known to have a mild laxative effect in high doses. Microcrystalline cellulose is a vegetable fiber used as a filler and binder in chewable tablets. Microcrystalline cellulose has good binding properties and can assist in forming firm tablets. Microcrystalline cellulose also imparts density to the tablets. The percentage of excipients in chewable tablets may vary depending on the specific formulation, the nature of the active ingredients, and the desired product characteristics. However, in general, the excipients in chewable tablets range from 30% to 80% of the total tablet weight.11-14

Binders are responsible for maintaining the shape and integrity of chewable tablets. They provide mechanical strength and prevent the tablets from being crushed or damaged when chewed. Examples of binders that are often used are Arabic gum, xanthan gum, hydroxypropyl methylcellulose (HPMC), and carbomer. Gum Arabic, also known as gum acacia, is a natural polysaccharide extracted from the Acacia tree. It has good binding properties and helps in forming firm chewable tablets. Gum Arabic also contributes to the softness and suppleness of the tablets. Xanthan gum is a polysaccharide produced by the bacterium Xanthomonas campestris. It has high water binding ability and forms a stable gel. Xanthan gum is used as a binder to increase the density and elasticity of chewable tablets. HPMC is a cellulose derivative that has good binding properties. It is frequently used in chewable tablet formulations because of its ability to form strong gels and impart mechanical strength to the tablets. HPMC can also
control the release of active ingredients from chewable tablets. Carbomers are synthetic polymers used as binders in chewable tablet formulations. It has the ability to form stable gels in the presence of water. Carbomers provide mechanical strength to tablets and assist in maintaining physical integrity during mastication.\textsuperscript{15}

The selection of the appropriate binder depends on the characteristics of the active ingredient, the desired physical properties of the chewable tablet, and the purpose of the particular formulation. In more complex formulations, a combination of binders can also be used to achieve optimal binding properties. The percentage of binder content in chewable tablets may vary depending on the specific formulation and desired product characteristics. Generally, the binder content in chewable tablets ranges from 1% to 10% of the total tablet weight.\textsuperscript{16}

Flavored fillers are used to give chewable tablets a pleasant taste. They can also be used to reduce the bitter or unpleasant taste of the active ingredient or other ingredients in a formulation. Flavoring ingredients can be natural or synthetic flavors such as mint, fruit, vanilla, or chocolate. Mint essential oil, such as peppermint oil or spearmint oil, is used to give chewable tablets a fresh, minty taste. Mint is often used in chewing gum and other chewable tablet products. Fruit flavor fillers are used to give chewable tablets a natural fruit taste. Examples of fruit flavor fillers include fruit extracts, fruit essential oils, or fruit flavor compounds. Vanilla extract or vanilla aroma compounds are used to impart a vanilla flavor to chewable tablets. Vanilla is one of the most popular flavors in chewable products, including chewable tablets. Flavor-filled chocolate is used to impart a distinctive chocolate flavor to chewable tablets. This can include ingredients such as cocoa powder, chocolate concentrate, or aroma compounds chocolate. The percentage of flavor filler content in chewable tablets may vary depending on the specific formulation and desired flavor intensity. Generally, the content of flavor fillers in chewable tablets ranges from 0.1% to 5% of the total tablet weight.\textsuperscript{17}

In addition, in the formulation of chewable tablets, it is necessary to pay attention to the proper processing techniques, such as granulation or drying, according to the nature of the natural ingredients used. Manufacturing methods such as wet or dry granulation can be used to produce chewable tablets that are consistent in texture, strength, and stability. Wet granulation or dry granulation methods can be used to produce chewable tablets that are consistent in terms of texture, strength, and stability. Wet granulation involves mixing the active ingredients and excipients in the presence of a binder liquid, such as water or an adhesive solution. This process produces moist granules, which are then dried and broken into smaller granules. These granules are then compressed into chewable tablets. The wet granulation method generally produces chewable tablets that have good hardness, high stability, and consistent disintegration time. Dry granulation involves mixing active ingredients and excipients without using a liquid binder. This process involves the use of pressure and friction to form granules. The resulting granules are then compressed into chewable tablets. The dry granulation method can produce chewable tablets with good strength but may require additional binders to achieve the desired texture and stability.\textsuperscript{18}

Sensory testing of the chewable tablets for which they are formulated is important to ensure that the tablets provide a pleasant user experience in terms of taste, texture, and chewability. Sensory testing may involve panelists or volunteers tasting and objectively evaluating the chewable tablets based on predetermined criteria. Evaluation of taste includes the intensity, type, and quality of taste felt by the panelists. For example, does the taste of the chewable tablet match the desired taste, is there an unwanted bitter, sour, or astringent taste. Texture evaluation involves assessing the firmness, hardness, or softness of the chewable tablet. Panelists can provide an assessment of the desired texture, for example, whether chewable tablets are easy to chew or too hard/soft. Elasticity is an important characteristic of chewable tablets. Panelists can provide an assessment
of the desired firmness in terms of elasticity, softness, or suppleness when chewed.\textsuperscript{19}

**Evaluation of chewable tablet preparations from extracts of natural ingredients**

In addition to considering stability and formulation, the safety and effectiveness of chewable tablets from natural extracts must also be evaluated through clinical trials and strict supervision. A clinical trial is a research process involving human participants to evaluate the safety, effectiveness, and tolerability of chewable tablets made from extracts of natural ingredients. Clinical trials were conducted according to research protocols approved by regulatory and ethical authorities. Clinical trials may involve observing patient response, monitoring side effects, measuring clinical parameters, and statistical analysis to assess product effectiveness. Chewable tablets from extracts of natural ingredients must be produced in compliance with applicable regulations and guidelines. Strict control involves monitoring the production, processing, and distribution of chewable tablets to ensure product quality, identity, safety, and purity. Strict supervision is carried out by regulatory authorities, such as the food and drug supervisory agency (BPOM), to ensure that products consumed by the public are safe and effective.\textsuperscript{20}

In evaluating safety, it is also necessary to consider possible side effects or interactions with other drugs. Potential side effects should be monitored and reported carefully. It is important to understand the safety profile of the product and provide clear information to potential users or consumers. Accurate and clear information regarding composition, recommended use, dosage, warnings, and contraindications must be included on product labels and packaging. This helps users or consumers in safe and proper use.\textsuperscript{20}

**4. Conclusion**

Formulation of chewable tablets from extracts of natural ingredients is an interesting approach in the development of pharmaceutical preparations. Through a selection of appropriate extracts, careful evaluation of stability, and attention to taste and aroma, these chewable tablets can provide significant benefits to patients. However, it is important to carry out careful research and testing to ensure the safety, effectiveness, and quality of these products before they are used in clinical practice.

**5. References**


