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A REVIEW ON MEDICATED LOLLIPOP: FORMULATION AND EVALUATION OF PIPERAZINE CITRATE MEDICATED LOLLIPOP.

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ABSTRACT:

Medicated lollipops represent an innovative oral drug delivery system that offers both therapeutic efficacy and improved patient compliance, especially in pediatric and geriatric populations. This review focuses on the formulation and evaluation of piperazine citrate medicated lollipops, aiming to explore their potential as a palatable and effective anthelmintic dosage form. Piperazine citrate, a well-known anthelminthic agent primarily used to treat intestinal worm infestations, faces challenges such as poor palatability and patient non-compliance when delivered via conventional oral dosage forms. The lollipop delivery system addresses these limitations by masking the drug's unpleasant taste, prolonging residence time in the oral cavity, and allowing partial pre-gastric absorption. This review discusses various formulation strategies, including selection of appropriate excipients, sweeteners, flavors, and polymers for controlled release, as well as manufacturing techniques such as molding and heating methods. Evaluation parameters such as drug content uniformity, hardness, friability, in vitro drug release, and stability studies are also critically examined. Furthermore, the potential for sugar-free and sustained-release formulations is highlighted to extend the application of this dosage form to broader patient populations. Overall, this review emphasizes the promise of piperazine citrate medicated lollipops as an effective alternative for conventional deworming therapies, offering improved compliance, efficacy, and patient acceptability.

Key word: Chloram, Lollipops, Candy, Confectionery, Medicated lollipop.

Introduction:

Oral drug delivery remains the most preferred and widely accepted route of administration due to its convenience, non-invasiveness, and ease of manufacturing. However, conventional oral dosage forms such as tablets, capsules, and syrups often pose challenges in pediatric and geriatric populations due to swallowing difficulties, poor palatability, and lack of patient compliance. To overcome these limitations, innovative drug delivery systems have been developed, among which medicated confectionery, particularly medicated lollipops, has gained increasing attention. Medicated lollipops combine therapeutic effectiveness with sensory appeal, making them an attractive option for delivering drugs in a patient-friendly manner.

Piperazine citrate is a commonly used anthelmintic agent for the treatment of intestinal helminth infections, particularly ascariasis and enterobiasis. It acts by causing neuromuscular blockade in helminths, leading to flaccid paralysis and eventual expulsion of the worms from the gastrointestinal tract. Despite its proven efficacy, the conventional administration of piperazine citrate, particularly in syrup or tablet form, is often associated with bitter taste and low patient adherence, especially among children. These drawbacks necessitate the development of novel delivery systems that improve acceptability and therapeutic outcomes.

The medicated lollipop offers an innovative alternative for piperazine citrate administration. It serves as both a delivery vehicle and a taste-masking platform, enabling easier and more enjoyable drug intake. Additionally, the extended retention time of lollipops in the oral cavity can enhance drug absorption via the buccal mucosa, thereby potentially improving bioavailability and onset of action. Furthermore, this dosage form can be tailored for immediate or sustained release profiles depending on the formulation components used, such as polymers and excipients.

The design and development of piperazine citrate medicated lollipops require careful consideration of various formulation parameters. Key aspects include the selection of appropriate sweeteners, flavoring agents, plasticizers, and binding agents to ensure effective taste masking, mechanical strength, and stability. The use of sugar-free alternatives can further extend the applicability of these formulations to diabetic patients and those on calorie-restricted diets. Manufacturing techniques such as heat-molding or compression methods must also be optimized to maintain drug integrity and uniform distribution.

This review aims to comprehensively explore the formulation strategies, technological approaches, and evaluation parameters involved in the development of piperazine citrate medicated lollipops. Emphasis is placed on both the scientific and patient-centric aspects of this novel dosage form, highlighting its potential to enhance therapeutic compliance, especially in vulnerable patient populations. In addition, the paper discusses current trends, challenges, and future perspectives in the development of medicated confectionery for systemic and local drug delivery

2.Overview of Piperazine citrate:

2.1 Mechanism of Action

Piperazine citrate is a widely used anthelmintic agent, particularly effective against intestinal nematodes such as Enterobius vermicularis (pinworms) and Ascaris lumbricoides (roundworms). Its anthelmintic activity is primarily attributed to its neuromuscular blocking action on helminths. Piperazine acts as a gamma-aminobutyric acid (GABA) agonist, stimulating inhibitory neurotransmission in nematodes, which leads to flaccid paralysis of the worms. This paralyzing effect prevents the worms from maintaining their grip on the intestinal wall, allowing them to be expelled from the gastrointestinal tract through natural peristalsis. Importantly, the drug has minimal effects on human GABA receptors due to species-specific receptor differences, thus ensuring a favorable safety profile.

2.2 Therapeutic Applications

Piperazine citrate is primarily indicated for the treatment of helminthic infections, including enterobiasis and ascariasis. It is especially favored in pediatric settings due to its relatively mild side effect profile compared to other anthelmintics. The drug is often available in oral dosage forms such as syrups, suspensions, and tablets, with a typical dosing regimen based on body weight. Its use is endorsed by the World Health Organization (WHO) as a part of public health deworming programs in areas with high helminth burden. Piperazine has also been used as a preventive therapy in high-risk populations where reinfection rates are common.

2.3 Limitations of Conventional Dosage Forms

Despite its efficacy, conventional dosage forms of piperazine citrate present several limitations, particularly in pediatric administration. Syrups and suspensions often require careful measurement and can suffer from poor palatability, which affects patient compliance, especially among children. Additionally, the bitter and salty taste of piperazine can lead to rejection by pediatric patients unless effectively masked. Tablets and capsules may be unsuitable for younger children who have difficulty swallowing solid oral dosage forms.

Another challenge lies in maintaining dose uniformity, especially in liquid formulations that may suffer from sedimentation or require frequent shaking. Furthermore, frequent dosing and the short half-life of the drug necessitate the development of more patient-friendly and compliant dosage forms. These drawbacks highlight the need for innovative delivery systems that improve both efficacy and patient adherence

3. Rationale for Medicated Lollipop:

3.1 Advantages in Drug Delivery

Medicated lollipops represent a novel and patient-friendly oral drug delivery system, especially beneficial for pediatric populations. The concept of delivering therapeutic agents via a confectionery base addresses multiple formulation challenges associated with conventional dosage forms. One of the primary advantages is controlled oropharyngeal drug release, which can improve drug absorption, especially for drugs intended for local action in the mouth or systemic absorption through the buccal mucosa.

This dosage form allows prolonged contact time between the drug and mucosal surfaces, which can enhance absorption and therapeutic efficacy. Additionally, lollipops are solid, portable, and stable under proper storage conditions, making them suitable for use in resource-limited settings or school-based deworming programs. From a formulation standpoint, they offer a flexible platform to incorporate flavoring, coloring, and sweetening agents to ensure a more acceptable taste profile.

3.2 Patient Compliance and Acceptability

One of the most compelling reasons for adopting a medicated lollipop form is the dramatic improvement in patient compliance, particularly in children who are often non-cooperative with syrups or tablets. The familiar and enjoyable form of a lollipop reduces the psychological resistance often associated with medicine intake. In many cases, children may perceive the lollipop as a treat rather than a medicine, thereby enhancing adherence without the need for coercion or parental intervention.

Additionally, the taste-masking capabilities inherent in the candy base of the lollipop allow for more effective delivery of bitter or metallic-tasting drugs like piperazine citrate. Unlike syrups that may still retain some bitterness, lollipops can incorporate multiple layers of flavors and sweeteners, such as sucralose, sorbitol, and fruit essences, to mask unpleasant drug tastes.

4. Formulation Aspect of Piperazine citrate lollipop:

4.1 Selection of Base and Sweeteners

Sugar-based lollipops typically use a combination of sucrose and liquid glucose to form a hard candy matrix. This base is heated to temperatures ranging from 135°C to 145°C to create a stable, non-crystalline structure upon cooling. Sucrose provides sweetness and bulk, while liquid glucose acts as a plasticizer, preventing crystallization and improving texture.

The choice of sugar-based ingredients is critical because piperazine citrate is heat-sensitive; thus, drug addition must be timed precisely to avoid degradation. The base must also provide sufficient hardness to support a stable dosage form and allow slow, controlled dissolution in the mouth.

4.2 Incorporation of Piperazine Citrate

Piperazine citrate is highly water-soluble and has a salty-bitter taste, which poses formulation challenges. In a lollipop, the drug should be added to the candy mass only after cooling the mixture to a safe range (approximately 90–100°C), to preserve the drug's stability. Uniform dispersion is essential to ensure dose consistency in each unit.

The dosage in pediatric lollipops typically ranges from 250 mg to 500 mg, depending on age and body weight. Because of the potential for thermal degradation, piperazine can be pre-dissolved in a small amount of water and incorporated into the base just before molding.

4.3 Flavoring and Taste Masking

Taste masking is a central challenge in formulating piperazine-containing lollipops due to the drug's characteristic bitter and salty profile. Several strategies' are employed to overcome this:

Use of strong fruit flavors (e.g. Pineapple, strawberry, orange, grape) that appeal to children

Citric acid to adjust pH and suppress bitterness.

4.4 Colorants and Appearance

The addition of FD&C-approved colorants improves visual appeal and helps in flavor identification (e.g., red for strawberry, orange for citrus). A bright and colorful appearance increases acceptability among children and ensures product differentiation.

4.5 Drug Stability and Compatibility

As piperazine citrate is sensitive to prolonged heating, the formulation process is optimized to reduce heat exposure. The drug should be evaluated for compatibility with excipients and stability at elevated processing temperatures. Packaging in moisture-resistant materials also helps preserve product integrity during storage.

Ingredients	**Quantity**	**Function**
Piperazine citrate	**100 mg**	**Active ingredient**
Glucose	**50g**	**Prevent crystallization**
Sucrose	**100g**	**Sweetener and structure**
Gelatin	**3g**	**Slow release**
Citric Acid	**1g**	**Ph adjuster**
Flavor	**1-2ml**	**Taste masking**
Colour	**As needed**	**Aesthetic appeal**
Purified water	**q.s**	**Vehicle**

5. Method of preparation of medicated lollipop: (Heat – Melt technique)

- Weigh sucrose and glucose with given quantity, add them to clean beaker.
- Add a small amount of purified water and heat gently with continuous stirring until mixture reaches app.130-140 0 c (Hard crack stage).
- Once a sugar base become clear and viscous add citric acid.
- Dissolve gelatin in water with gentle heating add add into sugar base with continuous staring.
- Dissolve Piperazine citrate in few warm water separately and mix into molten sugar base quickly.

- Add flavor and color, Mix uniformly.
- Allow to cool up to 60 to 80 0c then poor into lollipop molds containing sticks.
- Demold, wrap in moisture resistant packaging, and label appropriately.

6. Evaluation and Caracterization

Parameter	Method	Acceptance Criteria
Appearance	**visually**	**Absence of bubbles, cracks, or stickiness**
Hardness	**Monsanto hardness tester**	**4-8kg/cm2**
PH Measurement	**pH Meter**	**Typically 4.5-6.5**
Friability	**Roche Friabilator**	**<1%weight loss**
Thickness	**Vernier Caliper**	**± 5%**
Weight variation	**Weight 20 lollipops**	**As per USP max. diff.10 % each lollipop**
Drug content	**UV Spectrophotometer at 224 nm**	**90-110% of labeled claim**
Moisture content	**Loss on drying**	**<3%**
Dissolution study	**USP Dissolution apparatus**	**≥80% within 30 min**

7. Regulatory and safety considerations:

The development of a medicated lollipop containing piperazine citrate, particularly for pediatric use, must comply with regulatory standards to ensure product quality, safety, and therapeutic efficacy. Both formulation-specific regulations and active ingredient guidelines must be considered during product development and marketing.

7.1 Regulatory Classification

Medicated lollipops are classified as oral solid dosage forms and regulated as pharmaceutical preparations. In most countries, including those following FDA, EMA, or WHO guidelines, these products must meet criteria for:

- Content uniformity
- Stability
- Dissolution
- Microbial quality
- Labeling and dosage accuracy

7.2 Pediatric Use and Acceptability

Given that this dosage form is intended primarily for children, additional regulations related to pediatric safety, dosing accuracy, and palatability apply:
Child-resistant packaging may be required to prevent accidental overdose.
Toxicological data for excipients (e.g., artificial colorants, flavorings) must be reviewed for pediatric safety.
Acceptability studies involving sensory evaluation and ease-of-use are often recommended during pre-approval stages.

Piperazine citrate is a recognized anthelmintic agent, listed on the WHO Model List of Essential Medicines for Children, and its inclusion in lollipop form does not change its regulatory status but introduces a novel dosage form that must be justified through quality and safety data.

7.3 Excipients Safety and Limits

All excipients used, including sweeteners, colors, and flavors, must be within pharmacopeial limits (USP, BP, or IP). Some key safety considerations include:
Sucrose and glucose are generally recognized as safe (GRAS) but should be monitored in diabetic populations.
Artificial colors must be approved by relevant authorities and shown to be non-carcinogenic.
Citric acid and flavorings must not irritate the oral mucosa or lead to hypersensitivity.

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7.4 Quality Control Compliance

Good Manufacturing Practices (GMP) must be followed during production, including:
Batch record maintenance
In-process controls (temperature, mixing time, filling accuracy)
Finished product testing (drug content, hardness, dissolution)

8. Future Prospect:

The development of medicated lollipops as a novel drug delivery system is gaining momentum, especially for pediatric and geriatric populations. Piperazine citrate lollipops, in particular, offer great promise in addressing the challenges associated with conventional anthelmintic therapy. Future advancements in this area can significantly enhance therapeutic outcomes, patient adherence, and public health impact.

8.1 Integration of Advanced Drug Delivery Technologies

Incorporating controlled-release polymers, mucoadhesive agents, or nanoparticle-based carriers into the lollipop matrix can allow for more precise and prolonged release of piperazine citrate, reducing dosing frequency and improving efficacy. Such modifications may also reduce gastrointestinal side effects and enhance systemic bioavailability.

8.2 Expansion to Other APIs and Polytherapy Options

The medicated lollipop platform can be expanded to deliver combination therapies, such as piperazine citrate with albendazole or vitamin supplements, for broader-spectrum deworming or nutritional support. Dual-drug lollipops may offer a more holistic approach in community-based health programs.

8.3 Use in Mass Deworming Campaigns

Lollipop-based formulations may become particularly valuable in school-based and community-wide deworming initiatives. Their ease of use, acceptability, and stable shelf life make them ideal for large-scale distribution, especially in resource-limited settings.

8.4 Personalized and Smart Dosage Forms

Emerging technologies such as 3D printing of pharmaceuticals and dose-personalization could enable the production of tailor-made lollipops based on age, weight, or infection severity. Integration with digital health platforms may also allow for tracking medication adherence in pediatric populations.

8.5 Regulatory Framework and Global Adoption

As regulatory authorities begin to recognize the advantages of non-traditional oral dosage forms, clearer guidelines and fast-track pathways may emerge, facilitating broader approval and adoption of medicated lollipops. This may lead to increased investment and innovation in this space.

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10.Conclusion:

The formulation of piperazine citrate into a medicated lollipop presents a novel, effective, and patient-friendly approach to anthelmintic therapy, particularly suited for pediatric populations. Traditional dosage forms such as tablets and syrups often pose challenges in administration, especially for children who may resist bitter tastes or have difficulty swallowing. The lollipop dosage form not only improves compliance and palatability but also offers controlled release, enhanced taste masking, and ease of use.

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