A Review on Fast Dissolving Tablet
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ABSTRACT
Modern medicines require that pharmaceutical formulation be efficacious, safe, stable, and acceptable to oral dosage forms. This factor presents no great problem when drug is administered as a tablet or capsule which are designed to be swallowed as a unit. However, in that case where it is desirable to administer, as oral disintegrating tablets, chewable tablets or lozenges, taste acceptance particularly in pediatric preparations becomes a factor of prime consideration.

KEY WORDS: Styrene, divinyl benzene, Methacrylic acid, divinyl benzene

INTRODUCTION
Introduction to taste Masking:
In earlier times, the taste of medicine played an important role in curing of disease, more bitter drugs, the better and the cure. Nowadays concepts are totally changed. Patient expects the oral dosage form to be pleasantly flavored and palatable. This change in patient attitude is due to the advance made by flavoring and pharmaceutical industries. Today most of the drugs are unpalatable and unattractive in their natural state but modern pharmaceutical preparation present them to patient as colorful, flavorful formulation attractive to sight, smell and taste.¹

Taste is an important parameter governing compliance. Several of the oral pharmaceutical, numerous food and beverages products and bulking agents have unpleasant bitter taste. There are numerous over the counter (OTC) preparations that contain actives, which are bitter in taste. With respect to OTC preparations, such as cough and cold syrups, the bitterness of the preparation leads to lack of patient compliance.

In numerous cases, the bitter taste modality is an undesirable fruit of the product or formulation and considerably affects its acceptability by consumers. Bitter characteristic found in such system have been eliminated or minimized by various known processes, but no universally applicable technology for bitterness inhibition has
ever been recognized. The desire for improved palatability of these products has prompted the development of numerous formulations with improved performance and acceptability.

Palatability is a special requirement of oral medication in children, which in its broadest sense means acceptability, is most commonly associated with oral solid and liquid dosage form. It is also directly linked to the patient compliance, because if patient experiences apprehension and stress when medication is administered. It is likely that tend to avoid medication, which is needed to be taken chronically. Dosage form of pediatric patient requires particular attention to favorable palatability characteristics. Many children simply will not take medicines that are unpleasant and exhibit poor palatability. If the taste of a formulation is bad, it becomes impossible give to infants, neonates, and preschool child dose not like the taste. Pediatric preparation is generally flavored.

Modern medicines require that pharmaceutical formulation be efficacious safe stable and acceptable to oral dosage forms. This factor presents no great problem when drug is be administrated as a tablet or capsule which are designed to be swallow as a unit. However in that case where it is desirable to administer, as oral disintegrating tablets, chewable tablets or lozenges, taste acceptance particularly in pediatric preparation becomes a factor of prime consideration.²

Taste:

The biological definition of taste (gustation) is a chemical reaction derived from sensory responses from the four main taste perceptions: salt, sour, bitter, and sweet. Two other perceptions (umami and trigeminal) should be included when considering taste.³ Umami is derived from the presence of glutamate, such as monosodium glutamate, resulting in the fullness sensation from certain foods. Trigeminal is the burning sensation derived from such foods as spices and peppers. Figure 1.1 shows the location of the taste buds for these perceptions around the tongue.⁴

Sensations of taste are elicited by the tongue and interpreted by the brain. Certain areas of the respond more easily detected at the tip. bitterness is most readily detected at the back of the tongue. Sour sensation occurs at the sides of the tongue but salty sensations are usually detected at both the tip and at the sides of the tongue during ingestion taste buds react to soluble substances. The resulting sensation is transmitted to the brain by the ninth cranial (glossopharyngeal) nerve. The tenth and twelfth cranial nerves participate in this sensory reaction, but their role is limited.

The Physiology & Psychology of Taste:

To obtain an understanding of the reasoning behind this research, a basic understanding of the physiological and psychological events that
occur simultaneously in the experience known as taste is necessary. The earlier teaching of a taste map of the tongue showing distinct areas responding to certain stimuli has been replaced with a new theory. The most recent theory is that all taste buds respond to all stimuli. These stimuli include sweet, sour, bitter, salt, and umami. Taste stimuli are perceived through taste buds located on the tongue primary on the surface of the tongue. Humans have approximately 10000 taste buds, which appear in the fetus at about three months. In the infant, taste buds are found over the whole surface of the tongue, on the epiglottis, and on the insides of the cheeks. The taste buds present on the underside of the tongue, middle of the dorsal tongue surface, and inside of the cheeks. The taste buds present on the underside of the tongue, model of the dorsal tongue surface, and inside of the checks disappear gradually and are absent in the fully grown adult.

**Figure 1.2: Silkscreen images of human Taste sensation**

**Approaches of Taste Masking:**

**Sensory Approach:**
- Using flavoring and sweetening agents
- Inhibiting bitterness
- Numbing of taste buds
- Using Co₂ generating substance

**Complexation and Adsorption:**
- Complexation using ion exchange resins
- Formation of inclusion complexes with beta cyclodextrin derivatives
- Wax embedding of drugs

**Chemical Approach:**
- Formation of prodrugs
- Formation of different salts

**Barrier Approach:**
- Using microsphere or Microencapsulation
- Using viscosity modifier
- Using Emulsion
- Using liposomes

**Mechanism of action:**
- Synthetic Organic polymer comprising a hydrocarbon cross linked network to which ionizable group are attached have the ability to exchange ions attracted to
their ionized groups with ions of same charge present in solution. The resins may be either cation exchangers in which the resin insoluble group is acidic for example, sulphinic, carboxylic or phenolic groups, for anion exchangers in which the ionizable group is basic, either amine or quaternary ammonium groups.

The equation describing the formation of the drug resin complex as follows:

Cation Exchange resin:
\[ R-(COO^-)A^+ + B^+ \rightarrow R-(COO^-)B^+ + A^+ \] -------(1)

Anion Exchange resin:
\[ R-N(CH_3)_3^+ OH^- + X^- \rightarrow R-N(CH_3)_3^+ X^- + OH^- \] ------- (2)

Where \( B^+ \) and \( X^- \) represent the basic and acidic drugs respectively

\( R-(COO^-) A^+ \) and \( R-N(CH_3)_3^+ \) represents cationic and anionic exchange resin respectively.

Ion exchange resinate administered orally are likely to spend about two hours in the stomach in contact with an acidic fluid of the pH 1.2. The equation describing the equilibria in stomach is as follows:

Cation Exchange resin:
\[ R-(COO^-)B^+ + HCl \rightarrow R-(COO^-)H^+ + B^+Cl^- \] -------(1)

Anion Exchange resin:
\[ R-N(CH_3)_3^+ X^- + HCl \rightarrow R-N(CH_3)_3^+ Cl^- + H^+X^- \] -------(2)

Figure 1.3: schematic diagram of cation exchange resin

Figure 1.3 shows schematic diagram of a cation–exchange resin framework with exchange sites prior to and flowing an exchange reaction: (A) Initial state prior to exchange reaction with cation \( B^+ \); (B) Equilibrium state after exchange reaction with cation \( B^+ \).

Factors Affecting Loading of Drug onto Resins:

Cross linkage of Resin:
Cross linkage of Resins affects porosity and swelling properties of resins. Low crosslink age agents swell remarkably upon hydration. Higher grades have finer pore structure thus reducing loading efficiency with increase in cross linking. Low crosslink age increases the loading efficiency but also increases release rates 41

Particle Size:
Particle size does not have effect on drug loading. It affects only rate of exchange of ions species. The rate of exchange decreases with bead diameter due to reduction in diffusive path lengths hence larger particle size affords a slow release pattern 41
pH:
Protonated fractions of moderately weak acid or basic drug and weak functionality resin undergo change with pH changes thereby increasing/decreasing drug resin interaction and hence loading.\(^\text{42}\)

**Form of Resin:**
It was found that resins of H\(^+\) form have high loading capacity, as it possesses lower pH value than Na\(^+\). It has been found that drugs loaded onto H\(^+\) form of resin degrades while that a Na\(^+\) form does not degrade.\(^\text{42}\)

**Mixing speed:**
Drug loading was increases with increases the mixing speed at certain level further increases the speed can cause the complex was break and the drug loading was decreases.\(^\text{43,44}\)

**Size of exchanging ions:**
Larger the size of exchanging ions, slower will be the diffusion rates and release.\(^\text{45}\)

**Selectivity of Counter ions:**
The ions with low selectivity for resins such as H\(^+\) gets replaced easily resulting in higher drug loading.\(^\text{46}\)

**Mixing Time:**
Structural formula:

Drug loading increases rapidly in the initial 9 h and further increases between 20-30 h, probably because of surface absorptive phenomenon.\(^\text{46}\)

**Introduction to drug:**

**Generic name:** Cefuroxime axetil

**Description:** Cefuroxime is a semi-synthetic analog of cephalosphorin. It is a second-generation antibiotic. Cefuroxime axetil is of oral administration. Cefuroxime axetil has a broader spectrum of activity than cephalexin (first-generation). Cefuroxime is active against beta-lactamase producing strains of H.influenzae and N.gonorrhoeae, which are normally resistant to ampicillin and penicillin, respectively.


**Empirical formula:** C\(_{20}\)H\(_{22}\)N\(_4\)O\(_{10}\)S

**Molecular weight:** 510.48 g /mol

\[\text{pK}_a: 2.5\]

**Solubility:** Freely soluble in acetone, in alcohol very slightly soluble in water.

**Mechanism of action:** By binding to specific penicillin-binding proteins (PBP) located inside the bacterial cell wall, it inhibits the third and last stage of bacterial cell wall synthesis. Cell lysis is then mediated by bacterial cell wall autolytic enzymes such as autolysins; it is possible that cefuroxime interferes with an autolysin inhibitor.

**Pharmacodynamics/Kinetics**
Absorption: Oral (cefuroxime axetil): Increases with food
Distribution: Widely to body tissues and fluids; crosses blood-brain barrier; therapeutic concentrations achieved in CSF even when meninges are not inflamed
Protein binding: 33% to 50%
Bioavailability: Tablet: Fasting: 37%; Following food: 52%
Half-life elimination: Children 1-2 hours; Adults: 1-2 hours; prolonged with renal impairment
Time to peak, serum: I.M.: 15-60 minutes; I.V.: 2-3 minutes; Oral: Children: 3-4 hours; Adults: 2-3 hours
Excretion: Urine (66% to 100% as unchanged drug)

Uses:
Pharyngitis/Tonsillitis caused by Streptococcus pyogenes.
Cute Bacterial Otitis Media caused by Streptococcus pneumoniae, Haemophilus influenzae (including beta-lactamase-producing strains), Moraxella catarrhalis (including beta-lactamase-producing strains), or Streptococcus pyogenes.
Acute Bacterial Maxillary Sinusitis caused by Streptococcus pneumoniae or Haemophilus influenzae (non-beta-lactamase-producing strains only).

Taste masking of cefuroxime axetil
Cefuroxime axetil is a broad-spectrum cephalosporin antibiotics, prescribed extensively in both solid and liquid dosage forms, is extremely bitter resulting in poor patient compliance. Recently, a number of novel techniques for bitterness inhibition in formulations intended for pediatric and geriatric patients have been reported. Complexation with ion exchange resin is a simple and efficient technique of masking the bitterness.

In the present study, an attempt was made to mask bitter taste of cefuroxime axetil by Kyron T-114 (Cation exchange resin). It is a water-insoluble, high molecular weight; crosslinked polyacrylic acid cation exchange resin, which is a highly porous indigenous. Kyron T-114 is inexpensive and a simple, rapid and cost-effective material used for taste masking.

The natural variation in pH was used to prepare complexes that remain stable in the mouth without affecting gastric release. Various parameters affecting taste masking like drug: Resin ratios, amount of water, pH, stirring speed were optimized with efficient loading of cefuroxime axetil. The process of complexation was optimized using $3^2$ full factorial designs with reference to swelling time and stirring time.

The results of a $3^2$ full factorial design revealed that swelling time and stirring time significantly affected the dependent variable % drug loading. Batch A8 obtained was optimum drug loading compared to other batches as swelling time 45min and stirring time 4hrs. Thus, considering batch A8 as a promising candidate in terms of good taste masking properties and high % drug loadings and it was further used for tablets formulation. It is thus concluded that by adopting a systematic approach, an optimum point can be reached in the shortest time with minimum efforts. This approach can be utilized for taste masking of bitter pharmaceutical ingredients leading to improvement patient compliance.

The volunteers rated the final complexes (Batch A) as tasteless and agreeable. Drug release from DRC in salivary pH was insufficient to impart bitter taste. Complete drug release was observed at gastric pH in case of cefuroxime axetil.

Reference
1) Harmik S, Yamin S; Taste Masking Technologies in Oral Pharmaceuticals: Recent Developments and Approaches,


