Taste Masking

“bitter taste better”,

Taste masked products developed from innovative pharmaceutical technologies increase the commercial profits and create brand value for a company.
1. The flavor of a substance is attributed to its taste, sight, odor and qualities such as mouth feel.
2. Taste refers to a perception arising from the stimulation of taste buds present on the surface of the tongue.
3. Humans can distinguish among five components of taste: sourness, saltiness, sweetness, bitterness, and umami (savory)
Taste Masking

Taste masking technology filed in the period of year 1997 to 2007
Trend of taste masking technology filed in the period of year 1997 to 2007
It is one of the most efficient and commonly used taste masking technologies.

Coating can be done for tablets or for granules to be compressed into tablets, filled in capsules or suspended in a suspension.
**Coating**

**hydrophilic polymers:**
- hydroxyethyl cellulose
- hydroxypropyl methylcellulose
- copovidone (PVP)
- polyvinyl alcohol

**enteric polymers:**
- cellulose acetate phthalate

**reverse enteric polymer:**
- Eudragit EPO
- Eudragit E100

**water insoluble polymers:**
- ethylcellulose
- polyvinyl acetate
- crospovidone
- croscarmellose

**Lipids:**
- glyceryl palmitostearate
- Stearic acid

**Lipophilic vehicles:**
- vaseline and silicon oil for soft gel capsules

**gastrosoluble pore-formers:**
- inorganic or organic salts (calcium carbonate or magnesium oxide)

**Water soluble organic acids:**
- tartaric acid
- used with hydrophilic polymers to promote salivation to facilitate the formation of a viscous and mouldable particle paste to ease the swallowing of coated particles.
Multilayer coating

Overcomes coating imperfections especially for aggressively bitter drugs.

to attain a balance between the taste masking and in vitro release in solid dosage forms
Multilayer coating

Overcomes coating imperfections especially for aggressively bitter drugs.

A combination of enteric and reverse enteric polymers with pH independent polymer used for liquid suspensions with the pH maintained between 3.5 and to prevent the dissolution of polymers. This approach can provide an efficient taste masked suspensions over a long storage time.
Multilayer coating

Overcomes coating imperfections especially for aggressively bitter drugs.

Spacing layer (EC:PVP)

Taste masking layer (Eudragit E 100)

spacing layer overcomes the compatibility issues between the drug and excipients and can reduce the coating imperfections thereby improving the taste masking efficiency.
Overcomes coating imperfections especially for aggressively bitter drugs.

Multilayer coating

- Sugar coating
- Saliva-insoluble polymer
- A mixture of water soluble & insoluble polymers
Multilayer coating

Overcomes coating imperfections especially for aggressively bitter drugs.
Coating

Water soluble organic acids and their salts such as tartaric acid can be used with hydrophilic polymers coating. They promote salivation to facilitate the formation of a mouldable viscous mass with a slippery surface in contact with the saliva that considerably facilitates the swallowing of the composition even in high doses.

Sweeteners can be included in the coating solution for a better taste masking.

Acidic compounds such as citric and malic acid can be added to create an acidic microenvironment to promote the drug release in the upper intestine from the particles coated with reverse enteric polymers range.

Blend of water insoluble polymer (polyvinyl acetate) and a gastrosoluble polymer (aminoalkyl methacrylate copolymer) to achieve taste masking & fast drug release.
Granulation is an affordable, rapid and an easily scalable taste masking technology.
Granulation

**waxes:**
glycerol palmitostearate
glyceryl behenate
hydrogenated castor oil
beeswax

**swelling polymers** (During granulation, particle coating may remain incomplete. So, a swelling matrix can reduce the overall diffusion of the bitter active):
Microcrystalline cellulose
polycarbophil

**Flavors:**
sugar alcohol (erythritol)
Microencapsulation

**Applications**
- protection
- Taste masking
- Converting liquid to dry state
- Controlled release

**Methods of preparation**
- solvent extraction
- Solvent evaporation
- phase separation (coacervation)
- Spray drying
- Spray congealing

**Taste masking**: Converting liquid to dry state
Coating materials used in particulate coating are also commonly used for microencapsulation.

Microencapsulation is an advantageous taste masking strategy for suspensions due to the low particle size distribution of microcapsules that can remain suspended for a longer time.

The technique can be efficiently used for applying higher coating levels.
Sweeteners

Sweeteners are commonly used in combination with other taste masking technologies. They can be mixed with bitter taste medicaments to improve the taste of the core material which is prepared for further coating or may be added to the coating liquid.
Sweeteners

**Sugars:** raw sugar, glucose and caramel
**sugar alcohol** (sorbitol, xylitol, lactitol, maltitol or erythritol)
**sweeteners derived from plant parts**
Stevia
glycyrrhizin
Non sucrose component of sugar beet extract

**Synthetic sweeteners**
Sucralose improves taste without unpleasant, bitter/metalllic taste or after-taste
  Stable in the presence of hemostatic or dental etching agents (acidic environment) compared to aspartame
Less residue removed from the patient's tooth compared to sugar
Shows synergy of bitter taste masking effectiveness at Low pH (2 to 5)
**Aspartame**
saccharin sodium
acesulfame potassium
cyclamate
saccharin
Sweeteners

Sugars
- sucrose
- glucose
- caramel

Sugar alcohol
- sorbitol
- erythritol
- maltitol
- xylitol
- lactitol

Sweeteners of plant sources
- stevia
  - Honey leaf
- glycyrrhizin
  - 50-60 > sucrose
- Non sucrose component of sugar beet extract
  - flavor improving agent

Synthetic sweeteners
- Sucralose
- Aspartame
- cyclamate
- acesulfame K
- saccharin Na
  - after-taste perception
Taste Suppressants and Potentiators

**Bitter taste blockers**

- **Blockers**: compete with bitter substances to bind with the G-protein coupled (GPCR) receptor sites.
  - Lipoproteins
  - Phospholipids

- **Cooling & warming agents**: suppress unpleasant taste of medicament by subjecting taste receptors to extreme sensations to overpower the bitter taste and confuse the brain.
  - Cooling: eucalyptol
  - Warming: methyl salicylate

- **Suppressants**: do not have their own taste & work at very low concentration
  - Hydroxyflavanones
  - Their salts and stereoisomers
Taste Suppressants and Potentiators

**Potentiators**

increase the perception of the taste of sweeteners and mask the unpleasant after taste.

**Examples**

Thaumatine
neohesperidine
Dihydrochalcone (NHDC)
glycyrrhizin
Aldehydes (citral dimethyl acetal & henylacetaldehyde dimethylacetal)
Solid dispersion

Applications

interactions between the drug & hydrophobic polymers to decrease the solubility of a drug

Taste masking

interactions between poorly soluble drugs and hydrophilic polymers to increase the solubility of the drug

Hydrophobic polymers

Natural polymers

enteric polymers

long chain fatty acids

stearic & palmitic acid

shellac and zein

derivatives of acrylic acid polymers phthalate
Solid dispersion

This approach usually requires a higher concentration of excipients compared to other taste masking techniques.
Ion Exchange Resins

Are high molecular weight polymers with cationic and anionic functional groups. Resins form insoluble resinate through weak ionic bonding with oppositely charged drugs. After ingestion, the resinate exchange the drug with the counter ion in gastrointestinal tract and the drug is eluted to be absorbed

Example: Amberlite
Complex Formation

Cyclodextrins

• wraps the bad tasting molecule to inhibit its interaction with the taste buds
• interacts with the gatekeeper proteins of the taste buds

Sweeteners

such as acesulfame
Adsorbates

The drug may be adsorbed or/and entrapped in the matrix of the porous component, which may result in a delayed release of the bitter active during the transit through the oral cavity thereby achieving taste masking.
Viscosity Enhancers

Added to help masking highly bitter taste of suspended drug coated particles or microcapsules in liquid oral suspensions.

**Mechanism of action:**
• retard the migration of dissolved drug from the surface of the solid particle to the suspending medium.
• decrease the contact between the bitter medicament and the taste receptors

**Examples:**
xanthan gum, microcrystalline cellulose, Na carboxymethylcellulose, Hypromellose
pH Modifiers

pH Modifying agents are capable of generating a specific pH microenvironment in aqueous media that can facilitate *in situ precipitation of the bitter drug substance* in saliva thereby reducing the overall taste sensation for liquid dosage forms like suspension.
Factors Affecting Selection of Taste Masking Technology

1. Extent of Bitter Taste
2. Dose of Active Pharmaceuticals
3. Drug Particle Shape and Size Distribution
4. Dosage Forms
5. Drug Solubility
6. Ionic Characteristics of the Drug
Organoleptic properties

Sensory panel test

- Taste
- Flavor

- Type
- Level

-Human tester
-Scale from 1 to 5 for example
-measures should be taken to minimize bias in evaluation
-Not recommended to use elevated temperatures
Organoleptic properties

Measures to minimize bias in evaluation

- Determination of organoleptic capacity of the tester
- Ability to describe the flavor well
- Ability to duplicate results
- Ability to remember results
- Ability to detect new flavors (e.g., Due to interaction with container)
Electronic tongue is an instrument that measures and compares tastes.

**Organoleptic properties**
Mechanism involved for taste recognition in human and electronic tongue shows the same three levels:

1. the receptor level [taste buds in humans, lipid membrane of sensors in the electronic tongues]
2. the circuit level [neural transmission in humans, transducers in the electronic tongues]
3. the perceptual level [cognition in the thalamus in humans, statistical analysis by software in the electronic tongues].