

Various approaches toward taste masking: An overview

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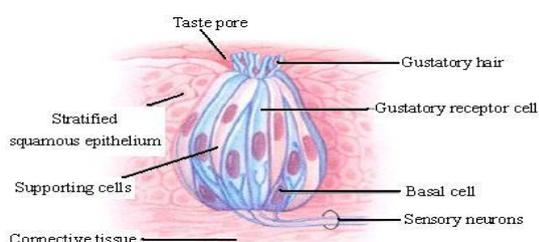
ABSTRACT

Taste masking is the process of masking the bitter taste of drug for improving the patient compliance. As the taste masking is for all the drug but it is mainly seen in the drug of pediatric & geriatric patient. Taste masking is improved by reducing the affinity of drug with taste receptor. Taste masking is done by application of polymer, amino acid, sweetening agent, & flavoring agent and also by removing of those group which are responsible for the bitter or unpleasant taste. To overcome this problem, many techniques have been developed to mask the bitter taste of drugs. These techniques are not only mask the bitter taste of drug but also enhance the bioavailability and performance of drug dosage form. It includes adding sugars, flavors, sweeteners, use of lipoproteins, numbing taste buds, granulation, use of adsorbates, coating drug, microencapsulation, multiple emulsion, viscosity modifier, vesicles and liposomes, prodrug and salt formation, inclusion and molecular complexes, solid dispersion and Ion Exchange Resins (IERS) which have been tried by the formulators to mask the unpleasant taste of the bitter drugs. The present review article highlights different technologies of taste masking with respect to dosage form and novel methods of evaluation of taste masking effect.

Keywords: Taste, Taste masking, Taste masking techniques, Taste evaluation, E-tongue

I. INTRODUCTION

Oral administration of bitter drugs with an acceptable degree of palatability is a key issue for health care providers, especially for pediatric patients [1]. Taste masking is defined as a perceived reduction of an undesirable taste that would otherwise exist. The ideal solution to reduce or inhibit bitterness is the discovery of a universal inhibitor of all bitter tasting substances that does not affect the other taste modalities such as sweetness or saltiness [2]. Taste-masking techniques are applied to mask or overcome the bitter or unpleasant taste of active pharmaceutical ingredients/drugs to achieve patient acceptability and compliance. Oral administration of bitter or unpleasant tasting drugs is often the biggest barrier for patient groups, such as pediatrics and geriatrics.



(Fig. 1: Anatomy and Physiology of taste bud)

In the past few years, significant progress has been made in the area of taste-masking by

applying novel strategies and techniques, such as hot-melt extrusion and microencapsulation. Masking of bitter taste of drugs is an important parameter for the improvement of patient compliance [3].

1.1. TASTE MASKING TECHNOLOGIES

Taste masking is defined as a perceived reduction of undesirable taste that would otherwise exist. Methods commonly used for taste masking involve various physical and chemical methods that prevent the interaction of taste buds with drugs. Two approaches are commonly utilized to overcome bad taste of the drug. Taste-masking techniques often go hand in hand with the formulation technology. In short, they need to be mutually compatible. For example, coated particles obtained after fluid-bed coating should be able to withstand the tablet compression process used for the final dosage form (tablet) manufacturing. The commonly used industrial techniques/methods of taste-masking include organoleptic methods, polymer coating, hot-melt extrusion, microencapsulation, complexation, and spray-drying.

1. By reducing the solubility of drug in the pH of saliva (5.6 - 6.8).
2. By altering the affinity and nature of drug which will interact with the taste receptor.

An ideal taste masking process and formulation should have the following properties.

- 1) Involve least number of equipments processing steps.
- 2) Effectively mask taste with as few excipients which are economically and easily available.
- 3) No adverse effect on drug bioavailability.
- 4) Least manufacturing cost.
- 5) Can be carried out at room temperature.
- 6) Require excipients that have high margin safety.
- 7) Rapid and easy to prepare [4, 5]

1.2. MATERIAL USED FOR COATING

- Synthetic polymers (Eudragits)
- Proteins, Gelatine, and Prolamines (Zein)
- Zeolites

It is classified based on the type of coating material, coating solvent system, and the number of coating layers. Hydrophobic polymers, lipids, sweeteners and hydrophilic polymers can be used as coating materials, either alone or in combination. Multilayer coating has been used to overcome the challenges of coating imperfections, which otherwise lead to a decline in the taste masking performance, especially for the aggressively bitter drugs. The core materials were coated with a first smooth and uniform spacing layer, which can minimize the coating imperfections during the second layer coating and can also act as an instant barrier between the taste receptors and the bitter core materials [6].

1.3. ORGANOLAPTIC METHODS

This is the simplest and most convenient method of taste-masking. It involves adding a combination of sweeteners (sucralose, aspartame) and flavors (orange, mint) to mask the unpleasant taste of low to moderately bitter actives. In addition, effervescent agents (sodium bicarbonate, citric acid) can also be added to improve the mouth feel. Some formulations may include a bitterness blocking agent that masks the bitter taste or the perception of bitter on the tongue. Such bitter blockers may include adenosine monophosphate, lipoproteins, or phospholipids. These agents compete with the bitter active to bind to the G-protein coupled receptors on the tongue (receptor sites that detect bitter), thus suppressing the bitter taste [7]. It has also been found that sodium chloride can be added to a formulation to mask bitterness as in the preparation of pioglitazone hydrochloride orally disintegrating tablets.

1.4. POLYMER COATING

The simplest option is direct coating that provides a physical barrier over the drug particles with a composition that is insoluble in the mouth. Hydrophobic or hydrophilic. Polymers, lipids, and

sweeteners can be used as coating materials, alone or in combination to produce a single or multi-layer coat. Methacrylic acid and methacrylic ester copolymers (Eudragit E-100, RL 30D, RS 30D, L30D-55, and NE 30D) have been effectively used for taste-masking with polymer coat levels varying from 10% to 40%, depending on the drug bitterness [8]. Fluid bed is often the technique of choice. Most recently, alternate approaches such as application of molten lipids [glyceryl palmitostearate (Precirol® ATO-5, Gattefosse, France) and glycerol behenate (Compritrol® 888-ATO, Gattefosse, France)] on the surface of drug particles has been used as a solvent-free alternative.

1.5. HOT MELT EXTRUSION

Hot-melt extrusion (HME) offers a relatively newer approach to taste-masking and provides advantages such as absence of organic solvents in the process, fewer processing steps, continuous operation, and scale-up capabilities [9]. For the purpose of taste-masking, the bitter active is mixed with other ingredients in a dry state. The mixture is filled in a hopper, conveyed, mixed, and melted by an extruder. The process subjects the materials to a heating process under intense mixing to obtain the taste-masked extrudates. The extrudate can then be milled or micronized to obtain taste-masked granules or particles, which are then incorporated into a suitable dosage form. Twin screw extruders are one of the most popular extruders and provide advantages such as short transit time, material feed, high shear kneading, and less over-heating.

1.6. MICROENCAPSULATION

Microencapsulation is a technology with a long history in the pharmaceutical industry, and taste-masking represents an expanded area of its application. In principle, microencapsulation provides the opportunity to encapsulate the bitter active and thus prevent its contact with taste buds. Microcaps is one such well-recognized technology that applies coacervation/phase separation to produce different encapsulated polymeric membranes. The process primarily consists of formation of three immiscible phases, formation of the coat, and deposition of the coat. The formation of the three immiscible phases is accomplished by dispersing the core particles in a polymer solution. A phase separation is then induced by change in the temperature of polymer solution; change in the pH, addition of a salt, non-solvent, or by inducing a polymer-polymer interaction. This leads to deposition of the polymer coat on the core material under constant stirring. The core particles coated by the polymer are then separated from the liquid phase by thermal, crosslinking, or desolvation techniques

leading to rigidization of the coat [10]. Microcaps are used in conjunction with Advatab compressed ODT technology.

1.7. COMPLEXATION

Cyclodextrins have been extensively used for taste-masking bitter drugs by forming inclusion complexes with the drug molecule. Cyclodextrins are unique bucket-shaped cyclic oligosaccharides containing at least six D-(+)-glucopyranose units attached by alpha-(1,4)-glucosidic bonds with a molecular structure of hydrophobic cavity and hydrophilic exterior. The formation of inclusion complexes and its type depends on several factors like drug properties, processes involved, the equilibrium kinetics, formulation excipients, and the desired final dosage form and delivery system. Taste masking is achieved by the interaction of cyclodextrins with proteins of the taste buds or by inhibiting the contact of bitter drug molecules with taste buds.

Ion exchange resins provide an alternative to cyclodextrins to achieve taste-masking by complexation [11]. Ion exchange resins are high molecular weight polymers with cationic and anionic functional groups. The preparation of the taste-masked complex involves suspending the resin in a solvent in which the drug is dissolved. The drug-resin complex formed is referred to as drug-resinate, which prevents direct contact of the drug with taste buds, thus providing taste-masking during administration. Upon ingestion, the resin exchanges the drug with the counter ion in the gastrointestinal tract, and the drug is released to be absorbed. Commercially available ion exchange resins that may be used for taste-masking are based on methacrylic acid-divinylbenzene polymer and styrene-divinylbenzene polymer.

1.8. SPRAY DRYING

Spray-drying provides an alternate approach to taste-masking by applying a physical barrier coating. The bitter drug is either dissolved or dispersed along with the polymer in a suitable solvent followed by spray-drying. The process usually

consists of three different steps: (1) atomization of feed into a spray, (2) spray-air contact (mixing and inflow) followed by drying, and (3) separation of dried product from the air. The process provides the option of using aqueous and non-aqueous solvents. The dried product often includes granules or beads containing taste-masked encapsulated drug. The amount of polymer coat can sometimes retard the drug release, and therefore requires careful polymer selection and process design to afford taste-masking. Also, the formulation and processing can affect whether or not the polymer is "coated" on the surface or dispersed. The quality of taste-masking depends on providing a co-dispersion. Some of the advantages of spray-drying include (a) less processing time being a single step process, (b) scale-up capability, and (c) wide variety in the choice of solvent and polymerate.

1.9. TASTE MASKING WITH FLAVOURS, SWEETENERS & AMINO ACID

This technique is the foremost and the simplest approach for taste masking, especially in the case of pediatric formulations, chewable tablets, and liquid formulations. But this approach is not very successful for highly bitter and highly water soluble drugs. Artificial sweeteners and flavors are generally being used along with other taste-masking techniques to improve the efficiency of these techniques. Numerous their combination because of its spicy and slight anesthetic effect. To support the taste masking capabilities of clove, honey vanilla or artificial vanilla flavor is preferred. Calcium carbonate, citric acid, or sodium bicarbonate may be included in the formulation if effervescence is required. Drugs, which can be taste masked by this composition, include acetaminophen, aspirin, ketoprofen, H₂-blockers, etc [12]. A composition comprising of anethole, eucalyptol (provides cooling, vapor action), and methyl salicylate (inhibits bitterness) can be used to mask the unpleasant taste of thymol, leaving the consumer with a pleasant taste perception [13]. Sodium citrate dihydrate, sodium saccharin, refined sugar, and flavors have been used to mask the bitter taste of ibuprofen when formulated as a syrup with pyridoxine HCl [14].

Table 1: Taste masking with flavors, sweeteners and amino acid

Sl. No.	Drug(s)/Active Agent(s)	Type of Formulation	Taste Masking Agent(s)
1	Eucalyptus oil	Mouthwashes	Fenchone, borneol, isoborneol
2	Aspirin	Medicated floss	Sodium phenolate
3	Thymol		-Anethole, eucalyptol and methyl salicylate
4	Ibuprofen	Syrup	Sodium citrate dehydrate, Saccharine & refined Sugar

1.10. TASTE MASKING WITH LIPOPHILIC VEHICLE

Oils, surfactants, polyalcohols, and lipids effectively increase the viscosity in the mouth and coat the taste buds, and therefore they are potential

tastemaskingagents. Guaifenesin has improved taste whenmixed with carnauba wax and magnesium aluminiumsilicate and then melt-granulated [15].The taste of cimetidine can be improved by granulating it with glyceryl monostearate [16].Gabapentin (acyclic amino acid, a drug for seizures) has improved taste whencoated with gelatin and then mixed with partially hydrogenated soybean oil and glyceryl monostearate [17].The taste of isoprothiolane can be masked by mixing it with hydrogenated oil at 80°C

and spraydried. The resulting granules are coated with hydroxypropyl methylcellulose. Acetaminophen granules are sprayed with molten stearyl stearate, mixed with suitable tablet excipientsand incorporated into a taste-masked, chewable tablet formulation. Bitterness-free syrup ofcarbetapentane citrate, diphenhydramine HCl acetaminophen, and Noscapine HCl can be formulated using polyglycerine fatty acid ester, glycerin, and chained triglycerides.

Table 2: Taste masking with lipophilic vehicle

S. No	Drug(s)/active agent(s)	Technique/formulation	Taste masking agent
1	Guaifenesin	Melt granulation	Carnauba wax and Magnesium aluminiumsilicate
2	Cimetidine	Granulation	Glyceryl monostearate
3	Gabapentin	Coating	Gelatin and mixture of partially hydrogenated soyabeen& GlycerylMonostearate
4	Isoprothiolane	Spray drying and coating	Hydrogenated oil and HPMC
5	Acetaminophen	Spraying/tablet	Molten stearylStearate
6	Acetaminophen, diphenhydramine, carbetapentane citratetriglycerides and noscapine HCl	syrup	poly fatty acid ester, glycerine& chained

1.11. TASTE MASKING WITH BY COATING WITH HYDROPHILIC VEHICLE

This is the simplest and most feasible option toachieve taste masking. The coating acts as a physicalbarrier to the drug particles, thereby minimizing interactionbetween the drug and taste buds. Coatingof chewable tablets provides excellent taste maskingwhile still providing acceptable bioavailability. A specialized technique, i.e., micro emulsion technology,has been used for taste masking of powders, chewabletablets, and liquid suspensions.

1.12. CARBOHYDRATES

The taste of orally administered drugs can be masked by coating the drug with carbohydrates. Bitter solid drugs such as pinaverium bromide, a spasmolytic, has no bitter taste when formulated in an organoleptically acceptable manner by polymer coating with amixture of cellulose or shellac and a second filmforming polymer soluble at pH less than 5 [18].A preparation of the anti-ulcerative drug propanthelinebromide is coated on low substituted sphericalhydroxypropyl cellulose and further coated with ethylcellulose to mask the unpleasant taste while readilyreleasing the active ingredients. Taste masking of ibuprofen has been successfully achieved by using their-suspension coating technique to form microcapsules,which comprise a pharmaceutical core ofcrystalline ibuprofen and a methacrylic acid copolymer(Eudragit) coating that provides chewable taste-maskedcharacteristics [19].

1.13. PROTEIN, GELATIN& PROLAMINES

Prolamines are zein, gliadin, and hordein. Various antibiotics, vitamins, dietary fibers,analgesics, enzymes, and hormones have been effectively taste masked using prolamine coatings. The taste masking is effective over a prolonged storage period. Besides effectively masking the taste of the bitter drug, prolamine coating does not affect the immediate bioavailability of the active substance. Zein or gliadin in combination with plasticizer were highly effective incontrolling the release of the active substance from the encapsulated particle and masking the unpleasant taste of the coated active substance [20]Granules consisting of cetraxate hydrochloride, corn starch, and Macrogol-6000 were coated with a mixture of Eudragit S-100, talc, and silica to mask bitter taste [21, 22].

Remoxipride, a D2-dopamine receptor antagonist, is well tolerated and completely absorbed after oral administration. Because of its extremely bitter taste, remoxipride is not a good candidate for oral administration. So, a palatable oral suspension of the drug was developed using microencapsulation, which provides complete bioavailability, but has a delayed absorptionrate of 3 h. In comparison, absorption was delayed only 1.6 h in a capsule form and only 1.0 h in an aqueous solution of 0.5% sodium lauryl sulfate.

1.14. ZEOLITE

Bactericidal feeds for domestic animals generally impart bitter taste to the formulation and

may create feeding aversion among the animals during the treatment [23]. To improve the taste of such formulations, the active agent (tiamulin fumarate) may be dissolved in methanol, supported on mordenite-type zeolite or starch, dried, and further premixed with the supports to produce sustained-

release, bitterness-free granules. The resulting formulation has stronger bactericidal effect on Mycoplasma, Staphylococcus, and Corynebacterium [24]. Given table summarizes taste masking of drugs by polymer coating.

Table 3: Tastemasking by coating with polymer

S. No	Drug(s)/active agent(s)	Technique	Polymer(s) used
1	Pinaverium bromide	Coating	Cellulose or shellac
2	Propantheline bromide	Coating	L-HPC, EC
3	Ibuprofen	Air-suspension coating	Eudragit
4	Triprolidine HCl	Dispersion coating	HPMC
5	Dimenhydrinate	-	Eudragit or CMC or starch
6	Cefanaldoxate HCl	Granulation and coating	PVP, EC, HPMC, Trisodium citrate
7	Enoxacin	Granulation and coating	HPC, HPMC, EC
8	Sparfloxacin and sucrose fatty acid ester mixture	Granulation and coating	L-HPC, EC, HMC/EC, HPMC, titanium dioxide

Note: HPMC: Hydroxypropyl methyl cellulose; HEC: Hydroxyethyl cellulose; HPC: Hydroxypropyl cellulose; L-HPC: Low substituted hydroxypropyl cellulose; CMC: Carboxy methyl cellulose; PVP: Polyvinyl pyrrolidone; EC: Ethyl cellulose; MCC: Microcrystalline cellulose; PEG: Polyethylene glycol

II. TASTE MASKING BY ION EXCHANGE RESINS

Ion-exchange resins (IERS) are high molecular weight polymers with cationic and anionic functional groups. The most frequently employed polymeric network is a copolymer of styrene and divinylbenzene. Ion-exchange resins are used in drug formulations to stabilize the sensitive components, sustain release of the drug, disintegrate tablets, and mask taste. Drug can be bound to the resin by either repeated exposure of the resin to the drug in a chromatographic column or by prolonged contact of resin with the drug solution. Drugs are attached to the oppositely charged resin substrate, forming insoluble adsorbates or resonates through weak ionic bonding

so that dissociation of the drug-resin complex does not occur under the salivary within the gastrointestinal tract (GIT). Drug molecules attached to the resin are released by exchanging with appropriately charged ions in the GIT, followed by diffusion of free drug molecule out of the resins.

Ion exchange resins can be classified into four major groups:

- . Strong acid cation-exchange resin.
- . Weak acid cation-exchange resin.
- . Strong base anion-exchange resin.
- . Weak base anion-exchange resin.

Strong acid cation resins (sulfonated styrene-divinylbenzene copolymer product) function throughout the entire pH range and can be used for masking the taste of basic drugs. Weak acid cation exchange resins function at pH values above 6.0. Similarly, strong base anion-exchange resins function throughout the entire range and can be used for masking the taste of acidic drugs, while the weak base anion exchange resins function well below pH 7.0 [25].

Table 4: Tastemasking with complexing agent & Ion exchange resins

S. No	Drug	Resin/complexing agent
1	Carbetapentane citrate	Cyclodextrin
2	Ibuprofen	Hydroxypropyl β-cyclodextrin
3	Gymnemasylvestre β-cyclodextrin	
4	Chlorpheniramine maleate	Indion CRP 244, indion CRP 254
5	Diphenhydramine HCl	Indion CRP 244, indion CRP 254
6	Buflomedil	Amberlite IRP 69
7	Orbifloxacin	Amberlite IRP 69
8	Chloroquine phosphate	Indion 234

2.1. TASTE MASKING APPROCHES & EVALUATION OF TASTE MASKING

- 1) Extent of the bitter taste of the API.
- 2) Required dose load.

- 3) Drug particulate shape and size distribution.
- 4) Drug solubility and ionic characteristics.
- 5) Required disintegration and dissolution rate of the finished product.

- 6) Desired bioavailability.
- 7) Desired release profile.
- 8) Required dosage form.
- 9) Taste masking absorption
- 11). Taste Masking with Lipophilic Vehicles lipids and lecithins
- 12). Taste Suppressants and Potentiators
- 13). Taste masking by gelation
- 14). Formation of salt and derivative
- 15). Use of Amino Acids and Protein Hydrolysates
- 16). Miscellaneous.
 - a) By effervescent agents
 - b) Rheological modification
 - c) Continuous multipurpose melt (CMT) technology
 - d) Wet Spherical Agglomeration (WSA)

2.3. EVALUATION

Taste, to think of, is a very subjective perception. Depending on individuals, the perceived taste may vary to different degrees. Quantitatively evaluate taste sensation, following methods have been reported in literature.

1. Panel testing (human subjects)
2. Measurement of frog taste nerve responses.
3. Multichannel taste sensor/ magic tongue
4. Spectrophotometric evaluation/ D30's value

2.4. A- IN VIVO TESTING

1. Panel testing (human subjects)

The panel testing is a psychophysical rating of the gustatory stimuli. In vivo taste evaluation carried out on a trained taste panel of 5-10 healthy volunteers organoleptic sense, with their prior consent. On placing the dosage form in mouth for 60 sec, bitterness recorded against pure drug using a numerical scale.

2.5. B- IN VITRO TESTING

1. Multichannel Taste Sensor / Magic tongue
Invention of "E-Tongue" electronic sensor array technology overcomes this problem, which is a device for recognition, quantitative multicomponent analysis and artificial assessment of taste and flavor. It recognizes three levels of biological taste including receptor level (Taste buds in humans, probe membranes in E-Tongue), circuit level (neural transmission in humans, transducer in E-Tongue), and perceptual level (cognition in the thalamus humans, computer and statistical analysis in the E-Tongue).

The probes consist of a silicon transistor with proprietary organic coatings, which govern the probe's sensitivity and selectivity, and measurement done potentiometrically. Each probe is cross selective to allow coverage of full taste profile and statistical software interprets the sensor data into taste patterns.

III. RECENT APPROACHES IN DEVELOPMENT OF TASTE MASKING

Yajima [26] developed a method of taste masking using a spray-congealing technique to mask the bitter taste of clarithromycin. Glyceryl monostearate and aminoalkyl methacrylate copolymer E (AMCE) were selected as ingredients. The palatability and taste of optimized formulation (CAM: GM: AMCE, 3:6:1) were significantly improved, compared with conventionally coated granules. Later, Yajima, Umeki, and Itai [27] evaluated the effects of operating conditions in the spray-congealing process on taste masking release and the micromeritics properties of clarithromycin wax matrix showed that the congealing speed of melt droplets was the dominant factor in masking the bitter taste of drug. Ishikawa et al. prepared and evaluated tablets containing bitter tasting granules masked by the compression method. Pirenzepine HCl and Oxybutynin HCl were used as model drugs and Eudragit E-100, microcrystalline cellulose, hydroxypropyl cellulose, and magnesium stearate were used as excipients. The results showed that there was rapid in vitro release of Oxybutynin and Pirenzepine at pH 1.2. The tablets disintegrated within 20 seconds into the saliva of the volunteers and they did not report a bitter taste after disintegration.

Tozaki et al. [28] developed a multichannel taste sensor system to detect the suppression of bitterness by sweet substances. Quinine was used as a bitter drug and sucrose as sweeteners. The results showed that the suppression of the bitterness of quinine by sucrose could be quantified by using the multichannel system.

Salazar de Saavedra and Saavedra Cuadra [29] developed and applied a sensorial response model to determine the design and taste of the oral liquid pharmaceutical dosage form. Acetaminophen was used as the model drug. It was found that a mixture of sweeteners and an essence was the most efficient way of masking the bitter taste of acetaminophen.

Pearnchob, Siepmann, and Bodmeier [30] investigated the potential of shellac to provide moisture protective and taste-masking coatings as well as extended-release matrix tablets. The efficiency of shellac to achieve moisture protection and taste masking was compared with that of hydroxypropyl methylcellulose (HPMC). The stability of acetylsalicylic acid was higher in tablets coated with shellac compared with HPMC-coated systems, irrespective of the storage humidity. Therefore, lower shellac coating levels were required to achieve the same degree of drug

protection. Shellac coatings also effectively mask the unpleasant taste of acetaminophen tablets.

Carbo et al. [31] developed a coating composition that masks the undesirable taste of a pharmaceutically active ingredient that is consumed orally. The coating composition has polyvinyl acetate, and a dimethylaminoethyl methacrylate and neutral methacrylic acid ester (Eudragit E100). Optionally, an alkaline modifier, such as triethanol amine may be included in the coating composition to enhance release of the active ingredient.

Meneaud, Al-ghazawi, and Elder developed a water dispersible formulation of Paroxetine for immediate oral administration. It comprises a dry blend of paroxetine, a water soluble dispersing agent (polyvinyl pyrrolidone/calcium carbonate/sodium starch glycolate), and a taste-masking agent (Eudragit L30D55/byclodextrin/lecithin/Polacrillin K) as a dispersible powder along with flavors and sweeteners.

Yu and Roche [32] formulated taste-masked pharmaceutical liquid formulations of Levofloxacin for oral administration. The liquid composition utilizes a "reverse enteric coating," which is soluble in the acidic pH of the stomach, generally about 1-4, but relatively insoluble at the nonacidic pH of the mouth. The coatings encapsulate the active ingredient and thereby effectively mask its taste and also provide for rapid release and absorption of the drug, which is generally desirable in the case of liquid dosage forms.

IV. FUTURE SCOPE OF TASTE MASKING

Bitter drug is a measure problem of paediatrics and children. Children cannot administer bitter drug so this approach is very useful to mask the bitter taste of drugs by resin complex. Resin forms insoluble complex with the drugs and complex form is palatable to the different age children. The drug release from complex is similar as drug is released from different formulations. In future this technique is very useful in masking of taste of many bitter drugs. The bitter drugs like Ofloxacin Hydrochloride, dicyclamine, hydrochloride, ciprofloxacin hydrochloride, Ofloxacin, Chloramphenicol can be easily handled with suspension, microemulsion, solid dispersion form without losing potency with good feeling effect in mouth. In future there may be modified with latest polymers in different grading system. Flavor may be added to the formulation to betterment of tastes. Bitter drugs are best for many disease so we can modify the formulations for treating the children with suitable additives. Eudragit grade polymer, resin complex are the good substitute to mask the taste of formulations used in paediatrics. SEM and TEM are the good technique for particles shape and

size and may be very useful tools in future to develop better agreement dosage form with nanoparticles. Nano particles are better absorbed from different dosage forms. Nano suspension and emulsions are formulated for better efficacy and tastiness to the patients. Patient agreement is important for the pharmacist to administer the drug so drugs are better designed and masked to the market for future development. Future scope of bitter drug masking will increase in broad sense in the industry and public in coming years.

V. CONCLUSION

Taste masking of bitter drugs has significantly improved the quality of treatment provided to suffering patients, especially children. There are so many effective techniques and methodologies that are constantly being researched and developed in the pharmaceutical field in response to the need of taste masking. Applicability of all these approaches varies from drug to drug and depends on the type of dosage form required. The ideal solution to bitterness reduction or inhibition is the discovery of a universal inhibitor of all bitter-tasting substances that does not affect the other taste modalities such as sweetness. But to date there is no single substance that acts as the universal inhibitor of a bitter taste. Research for the same has been performed for a long time. The type of technology used depends largely on the physical and chemical properties of the drug substance and the desired final dosage form. Advances in taste-masking technologies throughout the past few years have enabled the pharmaceutical industry to provide commercial products with improved patient acceptability and compliance, especially with pediatric and geriatric populations; along with enhanced convenience for patients on the go. More companies are turning to taste-masking expertise to complement their product portfolios for oral dosage forms. Lipoproteins composed of phosphatidic acids and beta-lactoglobulin [33]. It is also suggested that the multichannel taste sensor for the detection of suppression of bitterness by sweet substances [34] and other sensory evaluations of oral dosage forms of bitter drugs with taste inhibitors need to be further investigated for future applications. This would help in the development of more palatable and acceptable dosage forms.

REFERENCES

- [1]. S.B. Ahire, V.H. Bankar, P.D. Gayakwad and S.P. Pawar, A review: Taste masking techniques in pharmaceuticals, *Pharma Science Monitors*, 3(3), 2012, 68-82.
- [2]. S. Harmik, S. Yasmin, Kharand R.K, Taste masking technologies in oral

- pharmaceuticals: Recent developments and approaches, *Drug Development and Industrial Pharmacy*, 30(5), 2004, 429-448.
- [3]. A.K. Gupta, S. Madaan, M. Dalal, A. Kumar, D. N. Mishra, S.K. Singh and S. Verma, Taste masking technologies: A novel approach for the better patient compliance, *International Journal of Drug Delivery Technology*, 2(2), 2010, 56-61.
- [4]. D. Sharma, D. Kumar, M. Singh, G. Singh and M. S. Rathore. A review: Taste masking techniques in pharmaceuticals, a novel approach for the improvement of organoleptic property of pharmaceutical active substance, *International Research Journal of Pharmacy*, 3(4), 2012, 108-116.
- [5]. A. M. Suthar, Ion exchange resin impregnation method for taste masking: Review, *International Journal of Pharmaceutical Sciences*, 1(2), 2010, 6-11.
- [6]. P.R. Joseph, Evaluation of a taste sensor instrument (electronic tongue) for use in formulation development, *International Journal of Pharmaceutics*, 367, 2009, 65-72.
- [7]. V. Vummaneni and D. Nagpal, Taste-masking technologies: An overview and recent updates, *International Journal of Research in Pharmacy Biomedical Sciences*, 3(2), 2012, 510-524.
- [8]. K. Lehmann, H.U. Peterit and D. Dreher, Fast disintegrating controlled release tablets from coated particles, *Drugs Made in Germany*, 37(2), 1994, 53-60.
- [9]. F. Zhang, M.A. Repka, S. Thumma, S.B. Upadhye, S.K. Battu, J.W. McGinity and C. Martin, Pharmaceutical applications of hot-melt extrusion: Part I, *Drug Development and Industrial Pharmacy*, 33(9), 2007, 909-926.
- [10]. L. Lachman, H.A. Lieberman, J.A. Kanig, *The theory and practice of Industrial Pharmacy*. Vol. 1, 3rd edition. Philadelphia: PA; 1986; 420.
- [11]. S.H. Jeong and K. Park, Development of sustained release fast-disintegrating tablets using various polymer-coated ion-exchange resin complexes, *International Journal of Pharmaceutics*, 353, 2008, 195-204.
- [12]. E. Pandya, B. Harish, Callahan and P. Thomas, Taste masking for unpalatable formulations. US Patent No. 5,837,286, 1998.
- [13]. A.M. Montenegro, A.S. Mankoo and E. Brady, Taste masking of Thymol. Canadian Patent Application CA2228456, 1997.
- [14]. G.A. Depalmo, Composition based on Ibuprofen, for oral usage. European Patent Application EP0560207, 1993.
- [15]. R.F. Mozada, Medicament adsorbates and their preparation. European Patent Application EP0219458, 1987.
- [16]. E.F. Gottwald, H.P. Osterwald, H.M. Machoczek, and D. Mayron, Pharmaceutical compositions of Cimetidine. US Patent 5,057,319, 1991.
- [17]. T.L. Chau and S.R. Cherukuri, Delivery system for cyclic amino acids with improved taste, texture and compressibility. European Patent Application EP0458751, 1991.
- [18]. J. Block, A. Cassiere, and M.O. Christen, Galenic form. Germany Offen DE3900811, 1990.
- [19]. R.W. Shen, Taste masking of Ibuprofen by fluid bed coating. US Patent 5,552,152, 1996.
- [20]. Meyer and T.B. Mazer, Prolamine coating for taste masking of orally administrable medicaments. PCT International Application WO9312771, 1993.
- [21]. C. Haramiishi, Masked granule substance. JP 05,058,880, 1993.
- [22]. C. Haramiishi, Masked granule material. JP 05,194,193, 1993.
- [23]. R. Sjoebist, In-vivo validation of release rate and palatability of Remoxipride-modified release suspensions, *Pharmaceutical Research*, 10(7), 1993, 1020-1026.
- [24]. S. Ryu, Granular drug composition for animal. JP 03,101,619, 1991.
- [25]. A. Nanda, R. Kandarapu and S. Garg, An update on taste masking technologies for oral pharmaceuticals, *Indian Journal of Pharmaceutical Sciences*, 64(1), 2002, 10-17.
- [26]. T. Yajima, Particle design for taste masking using a spray congealing technique, *Chemical and Pharmaceutical Bulletin*, 44, 1997, 187-191.
- [27]. T. Yajima, N. Umeki and S. Itai, Optimum spray congealing conditions for masking the bitter taste of Clarithromycin in wax matrix, *Chemical and Pharmaceutical Bulletin*, 47(2), 1999, 220-225.
- [28]. S. Tozaki, K. Toko, K. Wada, H. Yamada and K. Toyoshima, Detection of suppression of bitterness by sweet substance using multi-channel taste sensor, *Journal of Pharmaceutical Sciences*, 87, 1998, 552-555.
- [29]. D. S. M. Salazar and C.I. Saavedra, Application of a sensorial response model to the design of an oral liquid pharmaceutical dosage form, *Drug Development and Industrial Pharmacy*, 26(1), 2000, 55-60.
- [30]. N. Pearnchob, J. Siepmann, and R. Bodmeier, Pharmaceutical applications of shellac: moisture-protective and taste-masking coatings and extended-release matrix

- tablets, *Drug Development and Industrial Pharmacy*, 29(8),2003, 925-938.
- [31]. M. Corbo, J. Desai, M. Patell and R. Warrick, Taste masking coating composition. US Patent 6,551,617, 2003.
- [32]. D. Yu, and E. Roche, Taste masked pharmaceutical liquid formulations. US 6,586,012, 2003.
- [33]. Y. Kasturagi, and K. Kurihara, Specific In-vitro bitter taste. *Nature*, 365 (6443),1993, 213-214.
- [34]. S. Tozaki, K. Toko, K. Wada, H. Yamada and K. Toyoshima, Detection of suppression of bitterness by sweet substance using multi-channel taste sensor, *Journal of Pharmaceutical Sciences*, 87, 1998, 552-555.