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Review Article

Pharmaceutics for effective drug dosage

Taste Masking of Pharmaceutical Formulations: Review on Technologies, Recent Trends and Patents

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Abstract: The majority of active pharmaceutical ingredients (APIs) found in oral dosage forms have unpleasant or obnoxious taste. Taste is one of the important parameters which governs patient compliance and also decides the success of a product in the market. Undesirable taste or the bitter taste is a major challenge that formulation scientist faces with many drugs. Hence, oral administration of bitter drugs is a big challenge, especially for pediatric patients. This article focuses on various tastes masking techniques by which the characteristics of the dosage form are improved and better patient compliance can be achieved. The article also discusses various recent taste masking evaluation techniques used in oral pharmaceutical formulations. The pharmaceutical companies are now engaged in developing novel techniques to overcome the problem of taste masking by numerous patents filed for taste masking. Lists of patents for taste masking are discussed and how these patents overcome the limitations of conventional approaches of taste masking is also reviewed. The present article also emphasizes various patented platform technologies based on different techniques used for taste masking. The important features and principles involved in taste-masking approaches of various patented technologies are also discussed. A better understanding of these new patents and patented technologies will help formulation scientists to select the most suited technology for development of new products with improved taste.

Keywords: Bitter drugs, Patient compliance, Taste masking techniques, Taste Evaluation, Patents, Platform technologies.

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1. INTRODUCTION

The human body is bestowed by natural organoleptic properties by nature. Taste sensation is one of them having the ability to detect taste of food, liquids and drugs. Now-a-days, taste masking is one of the major parameter governing patient compliance. Orally administered drugs are given to the patient in many dosage forms like capsules, tablets, granules and liquid forms like solutions or suspensions. Conventional tablets and capsules are meant to be swallowed whole, hence generally taste masking is not so much desired and in case of capsules the drug is enclosed within the tasteless gelatin shell. Children, older persons, often have trouble swallowing tablets or capsules. Hence, it is desirable to provide the drug either in dispersible solid form or as a liquid form. However if the drug has obnoxious and bitter taste they decreases the patient compliance.

1.1 ANATOMY OF TASTE BUDS

Humans receive tastes through sensory organs called tastbuds (also known as gustatory calyculi) concentrated on the upper surface of the tongue. Taste bud is onion-shaped and opens into an epithelial surface through a small opening called a taste pore. In mammals, taste buds are groups of 30-100 individual elongated "neuroepithelial" cells, which are surrounded in exclusive structure in the adjacent epithelium, termed taste papillae (Fig.1). Taste papillae can be seen on the tongue as little red dots, particularly at the front of the tongue[1]. There are four types of these papillae and each has its own specialized function. Figure 2 shows the four types of taste papillae. Four basic tastes are confirmed to specific regions of the tongue (Table 1) Taste buds are situated on the taste papillae. At the base of the taste bud, afferent taste nerve axons invade the bud and ramify extensively, each fibre typically synapsing with multiple receptor cells within the taste bud. In mammals, tastebuds are located throughout the oral cavity, in the pharynx, the laryngeal epiglottis and at the entrance of the esophagus[2].

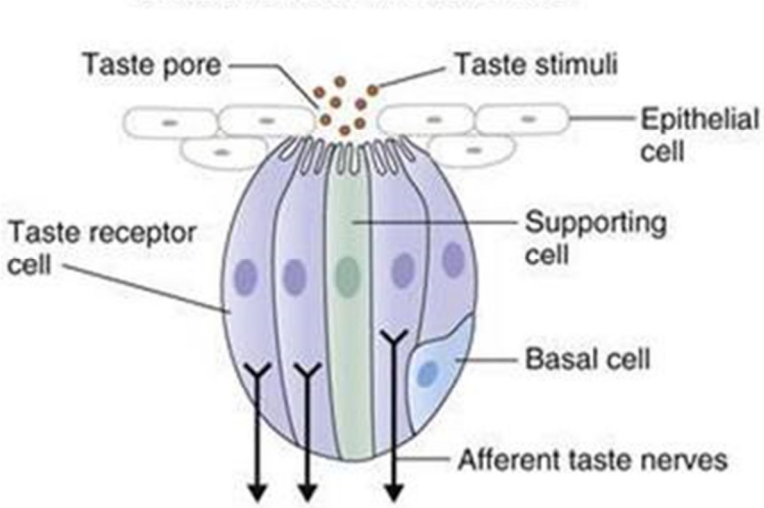

Fig1. *Structure of taste bud*

1.2 PHYSIOLOGY OF TASTE

As discussed earlier taste sensation is organoleptic property which results from chemical stimulation of receptor cells on taste buds[3]. Functionally receptor cells are of two types. First one is Ion channel type which allows the ions that give rise to the sensation of salty and sour. The sense of taste is conducted to the brain as chemical signals resulting from the ionic interactions, which causes electrical changes within the taste cells. Tastants alter the net negative charges of the taste cells causing increase in positive ion concentration within the taste cells which lead to depolarization and release of neurotransmitters [2]. Second type of receptor cells on taste buds are surface protein receptors which allows binding of tastants by a taste transduction process and gives rise to the sensation of sweet, bitter and umami. For bitter taste, the stimuli act as the binding between the tastants and G-protein coupled receptors in the cells, triggering the release of a G-protein called gustducin. Taste sensation begins when gustducin activates the effector enzymes phosphodiesterase1A. The effector enzymes then change the intracellular levels of second messengers such as cyclic adenosine monophosphate (cAMP), which release the calcium ions from the endoplasmic reticulum of the taste cell. The second messengers also activates sodium, potassium and calcium channels in the extracellular membrane. This ionization depolarizes the cell, causing the release of neurotransmitters that sends a nerve impulse to the brain that carries the signal of taste. The ninth cranial nerve of brain send resulting sensation with the help of which taste is detected. The different sensation to taste on tongue is greatly driven by factors like ageing and other parameters of an individual [4].

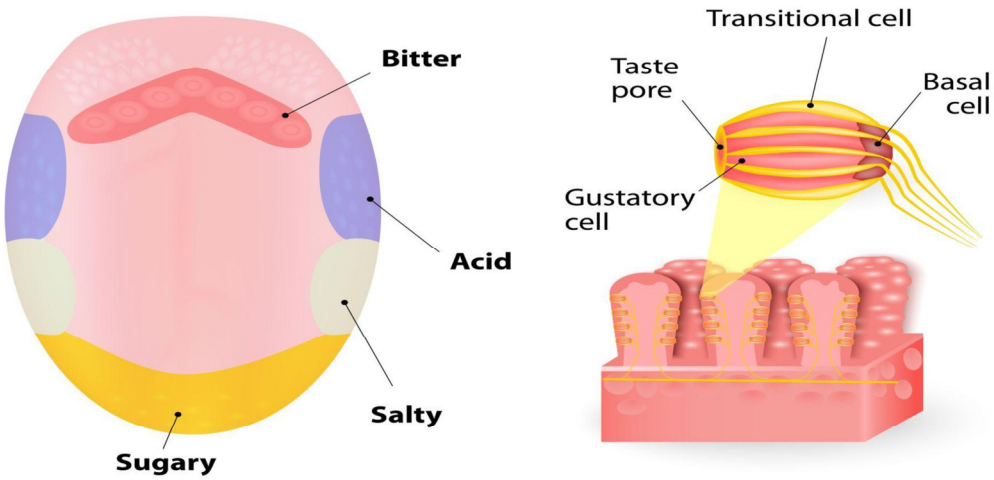

Fig 2. *Pictorial representation of Taste Receptors*

Table 1. Specific area of tongue and threshold concentration for primary taste sensations [5]

S.No	Flavour	Areaoftongue	Thresholdconcentration(%)
1	Sweet(sucrose)	Tip	0.5
2	Salt (NaCl)	Tip and sides	0.25
3	Sour (HCl)	Sides	0.007
4	Bitter (Quinine)	Back	0.00005

1.3 TASTE MASKING TECHNIQUES

Broadly, the taste masking approaches aim to use strong flavours, maskers and sweeteners to overpower the bitter active pharmaceutical ingredient (API), reduce contact between the API and the taste buds, or to reduce release of the API in the oral cavity [6]. To achieve the goal of taste abatement of bitter or unpleasant taste of the drug, various techniques reported in the literature shown in Table 2 are as follows [7]

i. Addition of flavoring and sweetening agents.
ii. Microencapsulation.
iii. Ion exchange resins.
iv. Formulation of inclusion complexes.
v. Bitterness inhibitors.
vi. Multiple emulsions.
vii. Prodrug approach.
viii. Gel formation.
ix. Development of liposomes.

Table 2. Taste masking approaches, substances and techniques used

S.No	Taste masking approach	Description	Substances and Techniques Used	References
1	Flavours and sweeteners	The Foremost and simplest approach for taste masking	Benzethonium chloride is used as dentifrice in stevia based sweetener.	8
2	Microencapsulation	It involves an application of a relatively thin coating to small bitter drug particles which can adapt to a wide variety of dosage forms and product applications. Coacervation phase separation, spray drying and fluid bed coating are common methods of microencapsulation	Sodium CMC is used to mask the bitter taste of ampicillin trihydrate powder by spray drying technique	9,10
3	Ion exchange resin complexation	Bitter tasting drugs can be attached to the oppositely charged resin substrate, forming insoluble adsorbates or resinates through weak ionic bonding	Amberlite IRP88 is used to mask the bitter taste of Paroxetine hydrochloride suspension	11-15
4	Cyclodextrin complexation	The drug molecule fits into the cavity of a complexing agent forming a stable complex which masks the bitter taste of a drug by either decreasing its oral solubility on ingestion or decreasing the amount of drug particles exposed to taste buds, thereby reducing the perception of bitter taste	β Cyclodextrin is used to mask the bitter taste of Zipeprol Antitussive syrup	16-19

5	Bitterness Inhibitors	Sodium salts such as sodium chloride, sodium acetate, sodium gluconate have been shown to be potent inhibitors of some bitter compounds.	Sodium salts such as sodium chloride, sodium acetate, sodium gluconate have been shown to be potent inhibitors of some bitter compounds.	10
6	Multiple emulsions	This system is mainly used for controlled-release delivery of pharmaceutical	These systems are mainly used for controlled-release delivery of pharmaceuticals. Both w/o/w or o/w/o multiple emulsion of chloroquine phosphate have been and partially effective in masking the bitter taste of drug.	20
7	Prodrug approach	By changing the molecular configuration of the parent molecule, the magnitude of a bitter taste response or taste receptor-substrate adsorption constant is modified.	The extremely bitter tasting antibiotics like chloramphenicol bitter taste is masked by forming chloramphenicol palmitate	20
8	Gel formation	Hydrolyzed gelatin and Water insoluble gels formed by sodium alginate in the presence of bivalent metals are also used to improve the taste and mouth feel when incorporated into small amounts in chewable tablets containing ingredients for taste masking.	Sodium alginate, carrageenan and macrogol-400 is used to mask bitter taste of Terfenadine	6,21
9	Development of Liposomes	Liposomes are carrier molecules comprising several layers of lipids, in which the bitter drug is entrapped within the lipid molecule	Phosphatidylcholine is used to masked the bitter taste of chloroquine phosphate in HEPES (N-2-Hydroxyethylpiperazine N-2)- ethane sulphonic acid buffer at pH 7.2	20

1.4 EVALUATION TECHNIQUE FOR TASTE MASKING

Depending on the dosage form selected and the technique incorporated to mask the bitter taste of the drug, below are some of the tests reported in various publications to evaluate the bitter taste of the formulation:

1. Dry powder-coated free films[22](For taste masking by polymer layering): Polymer powder is spread on a Teflon plate and the excess powder is scraped to achieve a uniform thick layer. This plate is then stored in an oven maintained at different temperatures (40, 60, 80 & 100^{0}C) for 1, 2, 4, 8, 12 & 24 hrs. The thickness of the dry film is then measured using a micrometre.
2. Thermal analysis of the polymer[22] (For taste masking by polymer layering): The thermal property such as Glass transition temperature of the polymer is characterized using Modulated Differential Scanning Calorimetry (MDSC).
3. Scanning Electron Micrographs[22](For taste masking by Microencapsulation): The surface and cross-sectional morphologies of the powder-coated films and film-coated tablets is evaluated using Scanning Electron Microscopy.
4. Evaluation of bitter taste threshold of API by subjecting formulations to human volunteers or Bitterness evaluation by Gustatory sensation test[23,24] Specified number of volunteers are subjected with the dispersion of bitter testing drug – qty 1ml (specified qty of API in water at specified solid concentration) which is held for 15 seconds before placing it mouth for 30 seconds.
5. Bitterness evaluation by Differential Scanning Calorimeter (DSC)[24]: Differential scanning calorimetry study of pure bitter-tasting drug and taste-masking polymer used in the study along with other formulation components is to be performed using Differential Scanning Calorimeter. All the samples accurately weighed, sealed in aluminium pan and heated at a scanning rate of 5^{0}C / min. Nitrogen is used as a purging gas with the flow rate set at around 40 mL / min. Aluminium pans and lid were used for all the samples, however an empty aluminium pan was used as a reference.
6. Bitterness evaluation by Fourier Transform Infra-red Spectroscopy (FTIR)[24]: IR transmission spectra for bitter-tasting drug is obtained using Fourier Transform Infrared Spectrophotometer. Bitter tasting drug or sample under study at 2% w/w concentration with respect to dry potassium bromide (KBr) and KBr is mixed and grounded into a fine powder using an agate mortar before compressing into KBr disc under a hydraulic press at 10,000 psi. This disc is then scanned 16 times at 4 nm/s at a resolution of 2 cm^{-1} over a specified wave number region in order to obtain or record characteristic peaks.
7. Bitterness evaluation by Scanning Electron Microscopy (SEM) [24] : The microparticles are mounted on brass stubs using carbon paste. SEM micrographs were taken using a scanning electron microscope at the required magnification at room temperature keeping working distance of 39mm and acceleration voltage of 5 kv, using the secondary electron image as the detector.
8. Drug Release of taste-masked formulation using Dissolution test [25] : Development of dissolution methods for orally disintegrating tablets is comparable to the approach taken for conventional tablets. It is good to have dissolution conditions similar to reference listed drugs as a starting point, however other dissolution media such as 0.1N hydrochloric acid. pH

4.5 acetate buffer and pH 6.8 phosphate buffer should also be evaluated. Literature search has indicated that USP 2 paddle apparatus is the most suitable & common choice for orally disintegrating tablets with a paddle speed of 50 rpm. Typically, dissolution of orally disintegrating tablets is very fast, it may be worth evaluating slower paddle speeds to obtain a profile. For larger tablets (more than one gram) or coated dense particles may produce a mound in the dissolution vessel which can be prevented by higher paddle speed. Therefore, a suitable range for paddle speed can be 25 to 75 rpm.

9. Bitterness evaluation by Electronic Tongue [26] : The main elements of an electronic taste-sensing system are a number of different sensor types attached to arm, a sample table, an amplifier, and a computer for data recording. Figure 3 gives a basic principle of electrochemical taste-sensing system[27]. This system imitates what is happening when molecules with specific taste nature interact with the taste buds on the human tongue. The taste buds are represented by sensors which interact with these molecules at the surface initiating changes in potential. These signals are compared with physiological action potentials which are recorded by computer, which correspond to the neural network at the physiological level. The data obtained can further be evaluated on the basis of already existing matrix of sensor responses which can be compared with human memory or association to already existing taste patterns.

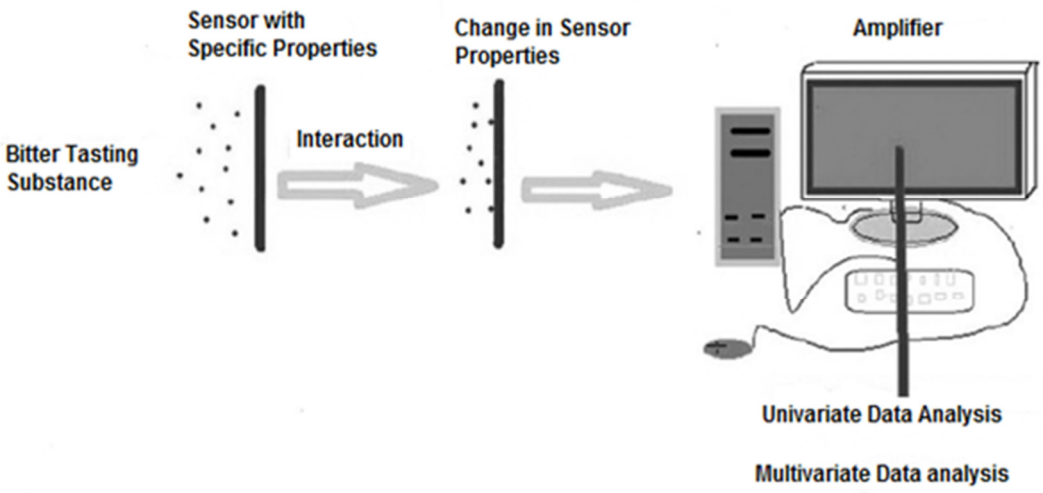

Fig 3. ***Electronic tongue: An analytical gustatory tool***

1.5 PATENTS ON TASTE MASKING FORMULATIONS

There are various patents reported on Taste masking formulations covering different types of taste masking techniques. Below table describes a few Patents and the techniques incorporated to mask the bitter taste of the drug (Table 3).

Table 3. ***Various patents reported on Taste masking formulations***

Patent number	Dateof Patent	Name of BitterDrug	Tastemaskingtechnique
US Patent 6,099,865	Aug, 8, 2000	Acetaminophen, Ibuprofen, Guaifenesin	Taste masking using Croscarmellose sodium (Bitter tasting drug is coated with CCS)
US Patent 6,596,311 B1	Jul, 22, 2003	Ibuprofen, Fluoxetine, Cimetidin	API coated with Cellulose acetate phthalate. These coated API is then formulated as a fast disintegrating tablet using other tableting ingredients.
US Patent 6,221,402 B1	Apr, 24, 2001	Sildenafil	Extruded spheronised pellets of active drug is coated first with aqueous soluble polymeric layer followed by aqueous insoluble polymeric layer. These coated beads are compressed along with other tableting agents such as fillers, disintegrants, sweeteners, flavours, lubricants, etc.
US Patent 4,800,087	Jan, 24, 1989	Acetaminophen	Microcapsules of about 10 microns to 1.5mm comprising of API + polymer mixture (poly methacrylic acid / poly methacrylic acid ester and acrylic acid esters) – coated with methacrylic acid esters copolymers and styrene acrylate copolymers. These coated particles are mixed with the ingredients of chewable tablets and compressed into tablets.
US Patent 5,075,114	Dec, 24, 1991	A mixture of Acetaminophen + Pseudoephedrin + Dextromethorphan +	Active ingredients are coated with Cellulose acetate / cellulose acetate butyrate + HPC as a pore former. These coated particles are mixed with other ingredients of chewable tablets

		Chlorpheniramine	such as Diluents + Sweeteners + Flavoursetc and compressed into tablets.
US Patent 5,607,697	Mar, 4, 1997	Dextromethorphan HBr and Chlorpheniramine Maleate	The bitter drug is mixed with tableting excipients such as Mannitol + Sorbitol + artificial sweeteners + Menthol + Sugar + Methyl salicylate + Saliva activated effervescent agent + Disintegrant + Lubricant – this mixture is compressed into tablet and coated with Ethylcellulose based organic film coating system.
US Patent 5,972,373	Oct, 26, 1999	Erythromycin & Clarithromycin	PolymerPolyvinylacetaldiethylaminoacetate + aminoalkylmethacrylate copolymer E) is either dissolved or dispersed in monoglyceride in β crystal form (Glycerylmonostearate) by heating and melting. This mixture is used to granulate API and dried granules of API is mixed with other tableting excipients and compressed into tablets.
US Patent 5,707,646	Jan, 13, 1998	Erythromycin & Clarithromycin	Active bitter drugs are mixed with functional polymer such as Eudragit E / Polyvinylacetaldiethylaminoacetate to form a complex. This complex is then mixed with other excipients such as sugar alcohol & basic oxide such as Magnesium oxide or Aluminium oxide to form a dry syrup.
US Patent 6,740,341 B1	May, 25, 2004	Dextromethorphan and Gatifloxacin	API either directly or after granulation using PVP K30 as a binder is screened through an appropriate screen to achieve the desired particle for further processing. This active particle is coated with spacing layer (either combination of Ethylcellulose + PVP or Ethylcellulose + HPMC) as a seal coat followed by reverse enteric polymer such as Eudragit E100 to achieve desired taste masking. These coated particles are then used to formulate taste masked dosage form.
US patent 4,916,161	Apr, 10, 1990	Ibuprofen	Active bitter drugs are granulated with HPMC-P. These active dried granules are then mixed with Alkalizing agent / buffering agents such as Alkali metal citrate ex: Potassium citrate + sweeteners + flavours + Lubricants, etc and compressed into tablets.
US Patent 5,028,632	Jul, 2, 1991	Aspirin	Tablet formulation comprising of active pharmaceutical ingredient + compacted spun fibers such as Maltose, Fructose, Sorbitol, Dextrose, Mannitol, Sucrose, Lactose or combination thereof + sedative agent such as Phenol + other tableting excipients – compressed into tablet. Ratio of Phenol to API to other excipients was 1 : 40 : 320.
US 2003/0032600 A1	Feb, 13, 2003	Levofloxacin Liquid composition	API + Flavouring agent + Sweeteners + Debittering agent + other liquid additives.
US 2005/0084540 A1	Apr, 21, 2005	Clarithromycin Oral suspension	API granules coated with Methacrylic acid copolymer and mixed with Sweeteners, Flavours and other additives.
US 6,514,492 B1	Feb, 04, 2003	Taste masking of Oral Quinolone (Orbifloxacin) liquid preparation using Ion-exchange resins	API - Cation ion-exchange resin complex formation.
US 6,565,877 B1	May, 20, 2003	Taste masked granules of Clarithromycin	By Solvent recovery method. API + Methacrylic acid co-polymer + HPMC P is dissolved in Acetone followed by recovery of taste-masked matrix from the solution thereof.
US 5,082,669 A	Jan, 21, 1992	Taste masking of Enoxacin granules	API coated with mixer of Ethylcellulose + HPMC.
US 6,767,557 B2	Jul, 27, 2004	Taste masked Pharmaceutical composition (Levofloxacin dry suspension for reconstitution)	API microencapsulated with Methacrylic Acid Copolymer.
US 6,165,512 A	Dec, 06, 2000	Dosage form containing Taste masked Acetaminophen	Extruded / Spheronised active beads coated with Ethylcellulose + HPMC based system, mixed with Glycerine free bodies to produce dosage form.

1.6 PATENTED TASTE MASKING TECHNOLOGY

Several pharmaceutical and drug delivery companies are currently engaged in providing patented commercial taste masking technology platforms for masking the bitter taste of medicament. Table 4 provides a list of these technologies along with their underlying principles.

Table 4. Patented commercial taste-masking technology

S.No	Taste Masking Technology	Name Of Company	Technology Used For Taste Masking	Marketed Product	References
1.	Microcaps ®	Aptalis Pharmaceuticals Technologies,USA	Microencapsulation (Each drug particle is completely encapsulated in a polymeric membrane using proprie-tarycoacervation phase separation technique)	AdvatabParacetamol® (Acetaminophen) ODT	28,29
2.	Opadry®	Colorcon Inc., USA	pH inde-pendent, water soluble film coating applied in an aqueous process.	Pseudoephedrine, Vitamins, Ibuprofen, Caffeine	30,31
3.	Flavorite®	Forte BV, Netherlands	Complex of uncoated flavor masking agents and viscosity enhancers	Paracetamol 125 Mg Powder For Suspension Kids, Azithromycin 200 mg/5ml Suspension	32
4.	OXP Zero ™	Oxford Pharmascience Group, Woodstock Road, Begbroke, Oxfordshire OX5 1PF, UK	Novel salt system where the drug is surrounded in a layered structure which protects the drug. Salt is insoluble in the mouth but readily releases the drug in the stomach.	OXP Zero ™ Ibuprofen Suspension Contain 100mg/5ml	33
5.	Fastmelt®	Athena Pharmaceutiques SAS, France	Microencapsulation (Masking The Bitter Or Pungent Taste Of Drugs Using Encapsulation Technology)	Cetirizine HCL 10 mg ODT Domperidone 10 mg ODT	34
6.	Camouflage ®	CambrexCorporation, USA	Microencapsulation	Gums, Aqueous Suspensions, Lozenges, Oral Disintegrating Tablets And Chewable TabLets	35
7.	Oralance®	OralancePharma, France	Molecular micro-incorporation	Wide range of final pharmaceutical forms such as Syrups, Dry Powder And Tablets.	36
8.	Micromask™	Particle Dynamics International	Microencapsulation	Micromask Ibuprofen 70%	37,38
9.	Kleptose® Linecaps	RoquetteFreres, France	Molecular encapsulation	Paracetamol	39

2. CONCLUSION

Taste masking is a very important factor affecting therapeutics. A lot of technologies are available not only for masking the unwanted taste of bitter drugs but also help to increase the palatability of formulation and patient compliance. Taste masking has now become avery important part of pharmaceutical product development because of increasing non compliance of patients; hence the pharmaceutical companies are now constantly developing new improved taste masking technologies to mask the bitter taste of drugs. In this review the most recent patents for taste masking are discussed and how these patents help to overcome the conventional approaches of taste masking are also discussed. The present article also provides an overview of various patented platform technologies based on different techniques used for taste masking. The method and principle involved in taste masking approaches used in various patented technologies are also highlighted. A better understanding of these new patents and patented technology will help researchers and formulators to select the most suited technology which will help to produce improved taste masked formulation. Microencapsulation, particle coating, film coating, cyclodextrincomplexation are some of the strategies used in patented technology platforms. The selection of appropriate patented taste masking technology depends on various factors like drug bitterness, dose of drug, drug solubility and dosage form. With the advent of new innovative taste masked technology it will provide great help to pharmaceutical formulators.

3. AUTHORS CONTRIBUTION STATEMENT

Mr Prashant Thakker gathered data, perceived the idea, carried out the research study with regard to this work. Dr. Jigna Shah and Dr Tejal Mehta guided in conducting this research study and also reviewed the manuscript. Dr.Gaurav Agarwal analysed the data and given necessary inputs towards the designing of the manuscript. All authors provided critical feedback, discussed the methodology, results and contributed to the final manuscript.

4. CONFLICT OF INTEREST

Conflict of interest declared none.

5. REFERENCES

1. Vummaneni V, Nagpal D. Taste masking technologies: an overview and recent updates. Int J Res Pharm Biomed Sci. 2012 Apr;3(2):510-24.
2. Pandey S, Kumar S, Prajapati SK, Madhav NS. An overview on taste physiology and masking of bitter drugs. Int J Pharm Biol Sci. 2010 Jul;1(3):1-.
3. Das SA, Srikanth L, Saha SU. Taste masking of ciprofloxacin by ion exchange resin. Int J Preclin Pharm Res. 2010;1(1):7-13.
4. Amita N, Garg S. An update on taste masking technologies for oral pharmaceuticals. Indian J Pharm Sci. 2002;64(1):10.
5. Sawan MS. Review on taste masking approaches in oral pharmaceutical dosage forms. Lebda Med J. 2016 Oct 20;1(1).
6. Sohi H, Sultana Y, Khar RK. Taste masking technologies in oral pharmaceuticals: recent developments and approaches. Drug Dev Ind Pharm. 2004 Jan 1;30(5):429-48. doi: 10.1081/ddc-120037477, PMID 15244079.
7. Gittings S, Turnbull N, Roberts CJ, Gershkovich P. Dissolution methodology for taste masked oral dosage forms. J Control Release. 2014 Jan 10;173:32-42. doi: 10.1016/j.jconrel.2013.10.030, PMID 24184344.
8. Kaushik D, Dureja H. Recent patents and patented technology platforms for pharmaceutical taste masking. Recent Pat Drug Deliv Formulation. 2014 Apr 1;8(1):37-45. doi: 10.2174/1872211308666140206150840, PMID 24499438.
9. Stange U, Führling C, Gieseler H. Taste masking of naproxen sodium granules by fluid-bed coating. Pharm Dev Technol. 2014 Mar 1;19(2):137-47. doi: 10.3109/10837450.2012.757784, PMID 23324020.
10. Sharma S, Lewis S. Taste masking technologies: a review. Int J Pharm Pharm Sci. 2010;2(2):6-13.
11. Yewale CP, Rathi MN, Kore GG, Jadhav GV, Wagh MP. Formulation and development of taste masked fast-disintegrating tablets (FDTs) of chlorpheniramine maleate using ion-exchange resins. Pharm Dev Technol. 2013 Apr 1;18(2):367-76. doi: 10.3109/10837450.2011.627870, PMID 22023351.
12. Kakumanu VK, Isloor S, Arora VK. Laboratories Ltd, assignee. Taste masked dosage forms of bitter tasting anti-retroviral drugs Ranbaxy, inventor. United States patent application US. Vol. 13(519); 2013 Jul 11. p. 025.
13. Shukla D, Chakraborty S, Singh S, Mishra B. Fabrication and evaluation of taste masked resinate of risperidone and its orally disintegrating tablets. Chem Pharm Bull (Tokyo). 2009 Apr 1;57(4):337-45. doi: 10.1248/cpb.57.337, PMID 19336927.
14. Bhise K, Shaikh S, Bora D. Taste mask, design and evaluation of an oral formulation using ion exchange resin as drug carrier. AAPS PharmSciTech. 2008 Jun 1;9(2):557-62. doi: 10.1208/s12249-008-9056-6, PMID 18491233.
15. Metcalf S, Purdy K. Assignee. Pharmaceutical formulation comprising a 2-amino acetamide derivative and an ion exchange resin Astra Zeneca UK Ltd, inventor. United States patent US. Vol. 6(193); 2001 Feb 27. p. 962.
16. Shah PP, Mashru RC. Palatable reconstitutable dry suspension of artemether for flexible pediatric dosing using cyclodextrin inclusion complexation. Pharm Dev Technol. 2010 Jun 1;15(3):276-85. doi: 10.3109/10837450903188485, PMID 22716468.
17. Ono NA, Miyamoto Y, Ishiguro T, Motoyama K, Hirayama F, Iohara D, Seo H, Tsuruta S, Arima H, Uekama K. Reduction of bitterness of antihistaminic drugs by complexation with β-cyclodextrins. J Pharm Sci. 2011 May 1;100(5):1935-43. doi: 10.1002/jps.22417, PMID 21374625.
18. Stojanov M, Wimmer R, Larsen KL. Study of the inclusion complexes formed between cetirizine and α-, β-, and γ-cyclodextrin and evaluation on their taste-masking properties. J Pharm Sci. 2011 Aug 1;100(8):3177-85. doi: 10.1002/jps.22539, PMID 21394723.
19. Roy GM. Taste masking in oral pharmaceuticals. Pharm Technol. 1994;18(4):84-.
20. Sonawane VM, Saiffee M, Shinde NY, Hawaldar AH, Pawar NA. An update of taste masking methods and evaluation techniques. Pharm Lett. 2010 Jan;2(6):1-5.
21. Chen JC, Bunick FJ, McNally G. Consumer Inc, assignee. Fast dissolving/disintegrating coating compositions Johnson J, inventor. United States patent US. Vol. 8(367); 2013 Feb 5. p. 104.
22. Cerea M, Zheng W, Young CR, McGinity JW. A novel powder coating process for attaining taste masking and moisture protective films applied to tablets. Int J Pharm. 2004 Jul 26;279(1-2):127-39. doi: 10.1016/j.ijpharm.2004.04.015, PMID 15234801.
23. Gao Y, Cui FD, Guan Y, Yang L, Wang YS, Zhang LN. Preparation of Roxithromycin-polymeric microspheres by the emulsion solvent diffusion method for taste masking. Int J Pharm. 2006 Aug 2;318(1-2):62-9. doi: 10.1016/j.ijpharm.2006.03.018, PMID 16647230.
24. Shah PP, Mashru RC, Rane YM, Thakkar A. Design and optimization of mefloquine hydrochloride microparticles for bitter taste masking. AAPS PharmSciTech. 2008 Jun 1;9(2):377-89. doi: 10.1208/s12249-008-9052-x, PMID 18431670.
25. Klancke J. Dissolution testing of orally disintegrating tablets. Diss Technol. 2003 May;10(2):6-9.
26. Rachid O, Simons FE, Rawas-Qalaji M, Simons KJ. An electronic tongue: evaluation of the masking efficacy of sweetening and/or flavoring agents on the bitter taste of epinephrine. AAPS PharmSciTech. 2010 Jun 1;11(2):550-7. doi: 10.1208/s12249-010-9402-3, PMID 20352537.
27. Latha RS, Lakshmi PK. Electronic tongue: an analytical gustatory tool. J Adv Pharm Technol Res. 2012 Jan;3(1):3-8. doi: 10.4103/2231-4040.93556, PMID 22470887.
28. Friend DR, Ng S, Sarabia RE, Weber TP, Geoffroy JM. Assignee. Taste-masked microcapsule compositions and methods of manufacture Adare Pharmaceuticals Inc, inventor. United States patent US. Vol. 6(139); 2000 Oct 31. p. 865.
29. Lai JW, Venkatesh G, Qian K. Assignee. Taste-masked pharmaceutical compositions with gastro soluble pore-formers VenkateshGopi M, Qian Ken K,

inventors. United States patent application US. Vol. 11(256); 2006 May 18. p. 653.
30. Porter SC, Woznicki EJ. Assignee. Maltodextrin coating ColorconInc, inventor. United States patent US. Vol. 4(643); 1987 Feb 17. p. 894.
31. Porter SC, Woznicki EJ. Assignee. Maltodextrin coating ColorconInc, inventor. United States patent US. Vol. 4(725); 1988 Feb 16. p. 441.
32. Recent patents on drug delivery & formulation. Kaushik D, Dureja H. Recent patents and patented technology platforms for pharmaceutical taste masking; 2014 [internet] [cited Nov 18, 2013]. Available from: http://www.forte-bv.nl/index.php?id=21.
33. Recent patents on drug delivery & formulation. Kaushik D, Dureja H. Recent patents and patented technology platforms for pharmaceutical taste masking; 2014 [Accessed on: November 24, 2013] [internet]. Available from: http://www.oxfordpharmascience.com/content/technologies/OxpZero.asp [cited 29/5/2020].
34. Recent patents on drug delivery & formulation. Kaushik D, Dureja H. Recent patents and patented technology platforms for pharmaceutical taste masking; 2014 [Accessed on Decembere 2, 2013] [internet]. Available from: http://www.ablpropharma.com/tastemask.html [cited 29/5/2020].
35. Recent patents on drug delivery & formulation. Kaushik D, Dureja H. Recent patents and patented technology platforms for pharmaceutical taste masking; 2014. Pdf [internet] [cited Sep 05, 2013]. Available from: http://www.cambrex.com/uploads/media/Cambrex_Drug_Delivery.
36. Raynal R, Lassu N, Brun-Baronnat C, Ioualalen K. Cochin, assignee. Non-ionizable hydrophobic galenical system Oralance Pharma Faculté De Médecine, inventor. United States patent application US. Vols. 12/532; 2010 Apr 8. p. 164.
37. Jeong SH. Development of sustained release fast-melting tablets using ion-exchange resin complexes (Doctoral dissertation, Purdue University).
38. Ther Deliv. Peter S. Taste-masked drugs in rupturing multiparticulates. US8236349; 2012 [internet] [cited Dec 06, 2013]. Available from: http://www.particledynamics.com/products/3_micromask.asp.
39. Ther Deliv. Yao. HP: Macdonald. Vol. X; 2013. 4th European paediatric formulation initiative conference [internet]. Haynes RB, Ackloo E, Sahota N [cited Dec 05, 2013]. Available from: http://www.roquette-pharma.com/media/deliacms/media//71/7171-0ec13e.pdf.