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Review Article

TASTE MASKING OF PEDIATRIC FORMULATION: A NEW PARADIGM

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ABSTRACT

Palatability of pediatric formulation is of greater importance when it comes to bitter active ingredients. So many advancements have taken place in the field of taste masking. Along with this they need to achieve global regulatory acceptability of such formulation is on the rise. This creates a situation where more children are in safe and effective medications. The main objective of this review article is to give a view on various tastes masking technologies employed in pharmaceutical field, their recent trends and pharmaceutical regulations.

Keywords: *Taste, Taste masking, Technologies.*

INTRODUCTION

Most active pharmaceutical ingredients (APIs) are highly bitter and this is the main difficulty behind the palatable preparation for pediatric therapy. Adult formulations can be easily taste masked by coating the tablet or by putting the drug in capsule dosage form, techniques which are not suitable for pediatric groups. For this three broad approaches have been used, these include to create a barrier between taste receptors and drug (physical coating, encapsulation); to make chemical or solubility modifications (controlling pH, esters of drug); and to overcome the unpleasant taste by adding flavors and sweeteners. Approaches have also been made to develop bitter blockers based on the biology of taste [1]. Many regulatory guidelines have been laid down for the pediatric class in the field of route of administration; excipients like additives, colorants and flavors; tolerance and safety; use of validated taste sensing analytical technologies etc. These all leads to better therapeutic compliance in pediatric therapy [2].

Taste Vs flavors

The five primary tastes are sweet, umami, sour, salt and bitter. Sweet chiefly at the tip, salt on the dorsum anteriorly, sour at the sides, and bitter at the back of the tongue[4]. Sweet and umami have one receptor, whereas bitter has about 25 receptors—called T2Rs. Taste receptors are located in

gustatory (oral) and non gustatory tissues, including the gut, brain, human airway smooth muscles, and reproductive tissues. Most of flavors and odors are perceived retronasally. Odors (chemicals) can reach the olfactory epithelium via the nose (orthonasal route) or mouth (retronasal route) and information is then sent to glomeruli in the olfactory bulb to mitral cells traveling to higher centers in the brain. In conclusion, "bad taste" is going to be an ongoing pediatric drug formulation problem because of the diverse number of receptors, the multiple transduction pathways, and age-related sensitivity based on genotype. Infants and children live in different sensory worlds, and there is a need for validation of taste assessment methods [3].

By addressing the taste factor early in the product development can make pharmaceutical company save much. In so doing, they can get their medications to market more quickly, ensure patient compliance, gain market leadership and reap generous economic rewards. They can also stay in compliance with the FDA's final rule, which went into effect December 2000 [5].

Taste masking

Using suitable agents one can reduce the unpleasant taste of bitter actives.But universally acceptable taste-masking technology does not seem to exist. Whereas aversion to bitter taste is universal. Many current tastes masking efforts are directed at reducing the negative attributes of pediatric dosage forms, which is a big challenge [2]. Finding a suitable taste masking method can impact the quality of taste masking and process effectiveness. There are many techniques developed for taste masking of bitter actives. These are as follows [6]:

- Addition of flavoring and sweetening agents.
- Complexation with Ion-exchange.
- Microencapsulation.
- Prodrug approach.
- Inclusion complexation.
- Granulation.
- Multiple emulsion technique
- Gel formation.
- Bitterness inhibitor.
- Miscellaneous.

Selection can be made based upon the type of drug, route of administration and compatibility of the active drug with a suitable masking agent.

Sweeteners

Different grades of sweeteners are available in order to control the taste. The following table 1 gives a compilation of most common artificial and natural sweeteners with their relative sweetness to sucrose and comments pertaining to each Artificial sweeteners like neohesperidine dehydrochloride, which is a

bitterness suppressor and flavor modifier elicits a very intense sweet taste. It is obtained by hydrogenation of bitter flavones neohesperidine.

Regulatory aspects

While formulating pediatric formulation, it has to be kept in mind that neonates and infants differs considerably from that of adults. They have differences in the metabolism and elimination of an ingredient with that of an adult [9].Several regulatory bodies like EmeA (European Medicines Agency) have made guidelines pertaining to their use. Additional information can be found in documents published by European commission[10][11] and US Food and Drug Administration (US FDA). Some regulatory information's made on some sweetener.

Sucrose

Sucrose is the most commonly used sweetening agent. It is a disaccharide that is readily hydrolyzed in the intestine to the absorbable mono-saccharides fructose and glucose. It should be avoided for pediatric patients suffering from hereditary fructose intolerance. Formulations with high amounts of sugar should be avoided in therapy of paediatric patients, suffering from diabetes[12]. For preparations intended for long-term therapy large amounts of sucrose should be replaced by sugar-free formulations, since sucrose causes a decrease in dental plaque pH, dissolving tooth enamel and promoting dental caries.

Fructose

Fructose causes an elevation in blood glucose concentration and should therefore be avoided in patients suffering from diabetes. It is also contraindicated in patients with hypoglycemia or hereditary fructose intolerance [13]. It may cause laxative effects when administered orally at high doses.

Recent trends

Masking of astringent taste of zinc in mouth washes like Listerine mouth wash was done with a combination of sweet note(Vanillin – ethyl vanillin), one fruity note (raspberry and lemon), one spicy note (ginger, clove, anise cinnamon or mixtures) and in combination with taste receptor blocker, which eliminated the burning sensation and astringency associated with eucalyptol and zinc [22].Coating agents like hydrogenated castor oil, Cremophor RH 40 identified as perfect coating agent for the receptor, because it masked the burns and produced end product [23]..

INDION 204 - weak acid cation exchange resin INDION 204 is a high molecular weight cross linked polymer. It is therefore not absorbed by body tissue and is totally safe for human consumption. It does not have any pronounced physiological action at recommended dosage levels and is definitely non-toxic.

Formation of inclusion complexes

Inclusion complex is a 'host-guest' relationship in which the host is complexing

agent and guest is the active moiety. The complexing agent is capable of masking bitter taste either by decreasing its oral solubility or decreasing the availability of drug to taste buds. Vanderwaal forces are mainly involved in inclusion complexes. The 'ring' is cylindrical, the outer surface being hydrophilic and the internal surface of the cavity being nonpolar. Appropriately sized lipophilic molecules can be accommodated wholly or partially in the complex, in which the host/guest ratio is usually 1:1, although other stoichiometries are possible, one, two or three CD molecules complexing with one or more drug molecules.Bitter taste of dimenhydrinate can be masked by forming a porous drug-polymer matrix [24, 25].

Smoothenol

Smoothenol is a portfolio of natural technology systems that enhance palatability of beverages by masking the undesirable off-notes and aftertaste commonly associated with sweeteners, caffeine, vitamins and minerals, nutraceutical and functional ingredients, and beverage bases. It's a product from Sensient Flavors LLC [26, 27].

CONCLUSION

To ensure that active ingredients is acceptable in formulations for pediatric use requires masking of undesirable bitter taste. And this need is the major concern for pharmaceutical companies to make patient compliance for their products. At the same time it should not compromise with safety and efficacy while in the race of developing a new pediatric formulation.

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