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Research Article

## INCREDIBLE TASTE MASKING OF CLARITHROMYCIN

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### ABSTRACT

Clarithromycin has poor acceptance by pediatric and geriatric patients due to bitter taste. Usually, in dry syrup formulations, high concentration of sugar is used for taste masking. But high consumption of sugar is related to several chronic diseases. Therefore, this study aimed to investigate taste masking capacity of excipients other than sugar. For this purpose, several granulating material were evaluated for masking bitter taste of clarithromycin. The best way to achieve pleasant taste was developed by using combination of aspartame and hydroxyl propyl cellulose which provided high intensity sweetness and miraculously reduced product bitterness.

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### INTRODUCTION:

The macrolide antibiotic, clarithromycin is extremely bitter in taste and effective in treatment of various infections in children and elderly patients, which often experience difficulty in swallowing solid oral dosage forms. For these patients, the drugs are mostly provided in liquid dosage forms, which lead to perceptible exposure of active ingredient to the taste buds. Taste masking is an important factor in these dosage forms for better patient compliance<sup>1</sup>.

Traditionally, taste masking in dry syrup formulations is done by using high concentration of sucrose, however, high sugar consumption has been a matter of great public and scientific interest. These adverse effects have been associated with obesity and risk of chronic disease like type 2 diabetes and cardiovascular diseases. As a result, many alternative taste masking agents have been extensively investigated. Non nutritive sugar can facilitate reduction in added sugar intake and promote beneficial effects on metabolic related parameters<sup>2,3</sup>. Aspartame has a taste profile very close to that of sucrose, presenting very low level of bitterness and sourness<sup>4</sup>. The study was planned to mask bitter taste of clarithromycin without use of sucrose. Different granulating materials were used to prepare clarithromycin granules by wet granulation technique and were dried, milled to obtain granule of desired

particle size. Extent of bitterness was evaluated by taste panel. It was recognized that clarithromycin granules prepared by HPC+ Aspartame mixture not only masked the bitter taste but also created a pleasant taste.

### MATERIALS AND METHODS:

Clarithromycin was received as gift sample from Amneal Laboratories Ltd.

Two different techniques were followed for taste masking:

(1) Solid dispersion technique: Solid dispersions of clarithromycin were prepared using Polyethylene glycol 4000 (PEG 4000) and with Polyvinyl Pyrrolidone K 30 (PVP 30).

Using PEG 4000:

Solid dispersion of clarithromycin with PEG 4000 was prepared in 4 different ratios i.e. 1:1, 1:2, 1:3 and 1:4. Clarithromycin was mixed with PEG 4000 in the ratio of 1:1, 1:2, 1:3 and 1:4. Sufficient quantity of acetone was added to dissolve the mixture and mixture was stirred on magnetic stirrer at 60°C-70°C to allow formation of solid dispersion. Solid dispersion obtained were further dried in fluid bed processor to obtain dried material which was further milled and passed through #16 to obtain granules.

Similarly, solid dispersions were also prepared using Polyvinyl pyrrolidone K30 in the ratio of 1:1, 1:2, 1:3 and 1:4.

(2) Granulation Technique 5 Different excipients were used separately for preparation of taste masking granules v.i.z. lactose, mannitol, sorbitol, starch, hydroxyl propyl cellulose. Using each excipients, granulation was performed in the ratio of 1:1, 1:2, 1:3 and 1:4.

Granulation with Lactose: Clarithromycin and lactose were sifted through # 30 sieve. Sieved lactose along with clarithromycin granulated using purified water as granulating agent. Wet granules were passed through # 10 sieve and were dried in fluid bed processor to form dried granules. Dried granules were milled and passed through # 16 sieve. Similarly granules were prepared in the ratio of 1:2, 1:3 and 1:4 ratio.

Also granules were also prepared separately using mannitol, sorbitol, starch and hydroxyl propyl cellulose. With each excipient, granules were prepared in the ratio of 1:1, 1:2, 1:3 and 1:4.

Taste Evaluation: The bitterness evaluation was performed on a taste panel of 6 human volunteers with mean age of 30 years. The volunteers rinsed their mouth thoroughly before and after the tasting. Granulated powder equivalent to 250 mg of clarithromycin was held in the mouth for 30 sec and then expectorated. Taste was evaluated and was assigned a numerical value ranging from 1 to 5 as mentioned in table 1, where high score indicated better taste masking. Results observed for taste evaluation score are mentioned in table 2.

Further different combinations of hydroxyl propyl cellulose were used along with intense sweetener aspartame to further conceal the bitter taste. Results of taste evaluation mentioned in table 3.

## RESULTS:

Solid dispersion were prepared by solvent evaporation method in which drug and inert excipients were dissolved in common solvent which was evaporated leading to the formation of solid dispersion. However, solid dispersion prepared with PEG 4000 or with PVP K 30 were unable to mask the bitter taste.

Taste masking by granulation technique was found to be comparatively better, inexpensive and quicker technique. Granulation lowers the effective surface area of the bitter substance that comes in contact the tongue. However taste masking effectiveness of different granulating agents was observed in the following order

Clarithromycin + PEG 4000  $\leq$  Clarithromycin + PVP K 30 < Clarithromycin + Sorbitol  $\leq$  Clarithromycin + Mannitol  $\leq$  Clarithromycin + Lactose Clarithromycin + Starch < Clarithromycin + Hydroxy Propyl Cellulose.

Reason for different taste masking capacity can be attributed to the solubility of granules in the saliva. Granules prepared with sorbitol and mannitol being easily soluble in saliva was not able to effectively mask the bitter taste, while granules prepared with hydroxyl propyl cellulose being less soluble had better ability to prevent the interaction of clarithromycin with taste receptors.

An interesting development in the taste masking was observed by using mixture of hydroxyl propyl cellulose with aspartame. Miraculously, granules were found to have no bitter taste when formulated with mixture of hydroxyl propyl cellulose with aspartame. Instead granules were having sweet and pleasant taste.

**Table 1:** Taste scale

Value	Parameter
5	Tasteless
4	Very Less Bitter
3	Moderate Bitter
2	Bitter
1	Strongly Bitter

**Table 2:** Results of taste evaluation score

Combination	Score				Mean Score
	1:1 ratio	1:2 ratio	1:3 ratio	1:4 ratio	
Clarithromycin + PEG 4000	1	1	1	1	1
Clarithromycin + PVP K 30	1	1	1	1	1
Clarithromycin + Lactose	2	2	2	3	2.25
Clarithromycin + Mannitol	2	2	2	2	2
Clarithromycin + Sorbitol	2	2	2	2	2
Clarithromycin + Starch	2	2	3	3	2.5
Clarithromycin + Hydroxy Propyl Cellulose	4	4	4	4	4

**Table 3:** Results of taste evaluation score

Combination	Score			Mean Score
	1:3+1 ratio	1:2+2 ratio	1:1+3 ratio	
Clarithromycin : Hydroxy Propyl Cellulose + Aspartame	4	5	5	4.66

**CONCLUSION:**

From the taste evaluation studies, it was concluded that miraculous taste masking for clarithromycin was achieved by granulation technique using combination of hydroxypropyl cellulose along with aspartame. These

granules can be used for further formulation of tablets, dry syrups and can also be taken for scale-up studies.

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