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Research Article

EVALUATION OF HOT MELT COATING AS TASTE MASKING TOOL

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ABSTRACT
In the present study, hot melt technique has been evaluated as a tool to mask bitter or unpleasant taste of Bromhexine hydrochloride and Salbutamol sulphate formulated as pellets. Bees wax and cetyl alcohol were evaluated as hot melt coating materials for taste masking. Drug containing pellets were prepared and coated using hot melt technique. Threshold bitterness concentrations of drugs and taste evaluation of hot melt coated pellets were determined by panel method. The pellets of all the formulation batches were in the size range of 825 to 995 µ after hot melt coating. Pellets exhibited uniformity of content in the range of 97.6 – 101.1%. Threshold bitterness concentration of both the drugs was found to be about 300 µg/ml. Amount of drug released from all pellets batches was less than threshold bitterness concentration for first 5 minutes indicating that taste of the drug was completely masked. Taste evaluation study of hot melt coated pellets by panel method revealed that about 80 % of the volunteers sensed no bitter taste even at 2 and 3% coating level whereas none of the volunteer reported bitter taste for pellets coated at 5%w/w level. Bees wax and cetyl alcohol both found to be better taste masking agents for Bromhexine hydrochloride and Salbutamol sulphate, when used by hot melt technique.

Keywords: Bees wax, Cetyl alcohol, Hot melt coating, Taste masking, Threshold bitterness, Panel method.

INTRODUCTION

The production and transmission of electrical impulses via the seventh, ninth and tenth cranial nerves from taste buds to those areas of brain which are devoted to the perception of taste, gives taste sensation.[1] Taste constitutes four primary effects, viz., sweet, sour, bitter and salty and perceived within 50 milliseconds. As the stimulus, taste is transmitted through water; water solubility is prerequisite for all tastes.[2,3]

More than 50% of pharmaceutical products are orally administered for convenience and economy. Unfortunately many drugs have unpleasant taste primarily bitterness. This has lead to dilemma for modern pharmaceutical science, as undesirable taste can hinder the acceptance and usefulness of many beneficial, safe and efficacious drugs. Thus elimination or reduction of bitterness is an important mainstay of product evaluation in oral pharmaceutical formulation. Proven methods for bitterness reduction and inhibition have resulted in improved palatability of the oral pharmaceuticals. Thus, taste masking of oral pharmaceuticals has become potential tool to improve patient compliance and commercial success of product.[4-6]

Various approaches have been used to mask the unpleasant taste of drugs.[7] It involves taste masking with flavors and sweeteners,[8,9] inhibiting bitterness,[10,11] numbing of taste buds,[5,12] prodrugs, formation of different salts,[4,13] complexation approaches, microencapsulation, multiple emulsion,[14] using viscosity modifiers,[15] vesicles and liposomes,[16] coating of drug particles with inert agents is simplest and most feasible option to achieve taste masking. The coating acts as a physical barrier to the drug particles, thereby minimizing interaction between the drug and taste buds. Various inert coating agents like starch, povidone, gelatin, methyl cellulose, ethyl cellulose etc. are used for coating drug particles.[17]

The objective of present study was to evaluate efficacy of hot melt coating as a tool to mask bitter or unpleasant taste of Bromhexine hydrochloride (BMH) and Salbutamol sulphate (SS) formulated as pellets. Bees wax and cetyl alcohol were evaluated as hot melt coating materials for taste masking.

MATERIALS AND METHODS

Bromhexin hydrochloride (BMH) was received as gift sample from Ven Petrochem and Pharma (India) Pvt. Ltd. and Salbutomol sulphate (SS) was generously gifted by Cipla Pvt. Ltd., India. Bees wax and cetyl alcohol were purchased from S. D. Fine Chemicals Mumbai. All other reagents were of analytical grade and used as received.

Preparation of Pellets

The composition of various batches of BMH and SS is given in Table 1. Pellets of drugs with microcrystalline cellulose (MCC Avicel PH 101) and lactose monohydrate were prepared by extrusion spheronization (Umang Pharmatech, India) using Povidone (PVP-K30) as a binder and water as granulating fluid. A damp mass was prepared by mixing drug, MCC and lactose and granulating it with binder solution. The damp mass was extruded through die-roller extruder. Extrudes were spheronized using spheronizer with 1.2 mm cross hatch plate at 900 rpm for 5 minutes. The pellets were dried at 60 °C for 4 hours.

Hot Melt Coating of Pellets

The waxes were melted in separate containers. Pre-weighed drug containing pellets were taken into the hot melt coating pan and allowed to attain a temperature of about 50 ºC. The molten wax was sprayed over tumbling pellets in small installments with constant rotation of pan. After each addition, pan was allowed to rotate for about 5 minutes further and then next installment of wax was sprayed. The coating level was determined by frequently taking weights of coated pellets to achieve desired coating level.

Evaluation of Pellets

Size Distribution

The size distribution was carried out using a sieve shaker and set of 4 ASTM sieves (#10, #14, #20 and #30) for 5 minutes. The size distribution expresses the efficiency of the process to manufacture the uniform sized pellets. Mean pellet size was calculated according to the following equation.[18]

d avg= $\sum$ % retained X Avg. sieve aperture/100

Crushing Strength and Friability of Pellets

The crushing strength of hot melt coated pellets was examined by Veego digital dial type hardness tester (Veego Scientific, India). For friability study, 1.0 g pre–weighed sample, collected on a sieve having 0.85 mm aperture with 25 glass beads (3 mm in diameter) were placed in a Roche friabilator (Veego Scientific India) and operated for 100 revolutions at speed of 25 rpm. The mass of pellets collected again on sieve with 0.85 mm aperture. The smaller particles were allowed to pass through the sieve and pellets were reweighed. The friability was determined as the percentage loss of mass of the pellets after test.[19]

Physical Parameters

For measuring bulk density, 25 g pellets of 14/20 mesh fraction were poured gently through a glass funnel into a 100 ml calibrated measuring cylinder. The surface was carefully made smooth and the volume occupied by the sample was recorded. The bulk density was calculated in g/ml. The tapped density was also measured in similar fashion as bulk density but the final volume was measured after the cylinder was tapped from the height of 3 inches until a constant volume was obtained. From the bulk and tapped density data, Compressibility index and Hausner ratio were calculated.

Drug Content

About 500 mg of pellets of both the drugs were ground carefully in mortar. The powdered mass equivalent to 50 mg of each drug was taken in 100 ml volumetric flask and 25 ml methanol for BMH and 25 ml of ethanol for SS was added. The drug was extracted by sonication for 10 minutes using laboratory sonicator (ISP Technologies, Mumbai). Volume was made up with distilled water, filtered and drug content was determined spectrophotometrically (Shimadzu-UV-150-02 Kyoto, Japan) at 314 nm and 295 nm for BMH and for SS respectively.

Evaluation of Taste Masking

Determination of Threshold Bitterness Concentration

A sensory test of the threshold value for the bitter taste of BMH and SS was carried out. For this purpose, 10 human volunteers were selected. They were asked to thoroughly rinse their mouth with purified water. Dilutions of both the drugs ranging from 50 to 500 µg/ml were prepared. Each volunteer was asked to hold 5 ml of drug solution in mouth for about 10 seconds, and then spat out.

The volunteers were asked to rinse their mouth after each sample tasting so as to remove any after taste of previous sample from mouth. The scores of bitterness for various dilutions of drug solution were given by 10 volunteers as compared to distilled water. Minimum concentration level of drug which was judged as very bitter by the volunteers was considered as bitterness threshold.[20,21]

Hot melt coated pellets equivalent to 50 mg of drugs were separately added in a flask containing 10 ml of pH 6.8 buffer solution, constantly stirred by magnetic stirrer and maintained at 37 °C. After 30 seconds, 1 ml of buffer solution was withdrawn from the flask, diluted to 100 ml and absorbance was taken spectrophotometrically. The taste evaluation was carried out for 10 minutes.

Taste Evaluation by Panel Method

The taste of coated pellets was checked by panel method. For this purpose, 10 human volunteers were selected. Their mouth was thoroughly rinsed with purified water. Pellets equivalent to about 50 mg of drug were placed on tongue and taste was evaluated after 10 seconds. Taking the taste of pure drug as standard, the degree of bitterness of drug complexes

was judged by volunteers according to above mentioned bitterness scale.

RESULTS AND DISCUSSION

Evaluation of Pellets

The pellets prepared by extrusion spheronization show very good micromeritic properties. Pellets appear with smooth surface on visual observation. All the formulations were in the size range of 825 to 995 µ after hot melt coating. The lower values of angle of repose, carr's compressibility index and Hausner ratio of all the formulation batches indicate good flow properties. The friability was negligible with the maximum value being 0.27 %. This value can be attributed to the loosening of some wax from the coating due to attrition with friability test apparatus. The hardness of pellets was in the range of 1.30-1.87 kg/cm^2. Both these values indicate that the pellets were having good mechanical strength. Drug content in the pellets from all the formulation batches found to be in the range of 97.6 – 101.1% which indicates uniformity of actives in formulations.

Taste Evaluation Studies

Determination of Threshold Bitterness Concentration

Taste evaluation was carried out by analytical method. Threshold bitterness concentration of both the drugs was determined and was found to be about 300 µg/ml, all the volunteers reported maximum bitterness at this concentration.

The amount of drug released from all pellets batches was found to be less than threshold bitterness concentration for first 5 minutes indicating that taste of the drug was completely masked when formulated as hot melt coated pellets.

Taste Evaluation Studies by Panel Method

The results of taste evaluation by panel method are shown in Table 4.

Taste evaluation study of hot melt coated pellets by panel method revealed that about 80 % of the volunteers sensed no bitter taste even at 2 and 3% coating level whereas none of the volunteer reported bitter taste for pellets coated at 5%w/w level. The reason for this may be that, at 2 and 3%w/w level, the coating may be non uniform and insufficient to coat pellets completely resulting in incomplete masking of bitter taste.

CONCLUSION

From the present study, it can be concluded that, both the waxes Bees wax and Cetyl alcohol are equally efficient in masking bitter taste of the drugs by hot melt coating. The coating level of above 3%w/w is required to mask the complete bitter taste of drugs as indicated by the study. Thus the hot melt coating can be an effective, less time consuming, eco-friendly and economic mean for preparing taste masked pellet formulations of bitter drugs.

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REFERENCES

1. Reilly WJ. Pharmaceutical necessities. In: Remington: The science and practice of pharmacy. 20th ed. Easton: Mack publishing company; 2002. p. 1018-1020.
2. Gowthamarajan K, Kulkarni GT, Kumar NM. Pop the bitter pills: Taste masking technologies for bitter drugs. Resonance 2004; 25-32.
3. Shallenberger RS. Taste recognition chemistry. Pure & Appl Chem 1997; 69(4):659-666.
4. Nanda A, Kandarapu R, Garg S. An update on taste masking technologies for oral pharmaceuticals. Indian J Pharm Sci 2002; 64(1):10-17.
5. Roy GM. Taste Masking in Oral Pharmaceuticals. Pharm Tech 1994; 18(4):84-99.
6. Kleinert HD, Baker WR, Stein HH. Orally bioavailable peptidelike molecules: a case history. BioPharm 1993; 6(1):36.
7. Hiremath JG, Shastry CS, Srinath MS. Pharmaceutical approaches of taste masking in oral dosage forms. Indian Drugs 2004; 41(5):253-257.
8. Y. Matsubara, A. Kawajiri, and F. Ishiguro. Granules with Suppressed Bitterness. JP Patent 02056416. February 26, 1990.
9. G.A. Eby. III Taste-Masked Zinc Acetate Compositions for Oral Absorption. US Patent 5095035. March 10, 1992.
10. Katsuragi Y, Sugiura Y, Lee C, Otsugi K, Kurihara K. Selective inhibition of bitter taste of various drugs by lipoprotein. Pharm Res 1995; 12(5):658-662.
11. SL Nelson. Inhibiting undesirable taste in oral composition. US Patent 5766622. June 16, 1998.
12. JA Reimer. Bitterness inhibitors. US Patent 5336513. August 9, 1994.
13. S. Motola, AR Branfman, GR Agisim and DJ Quirk. Acid addition salt of ibuprofen and meglumin. US Patent 5028625. July 2, 1991.
14. Rosoff M. Pharmaceutical dosage form disperse system. Vol. 1. New York: Marcel Dekker, Inc; 1988; p. 245-283.
15. Y. Kawasaki, and Y. Suzuki. Acetaminophen or Phenobarbital Syrup compostion. US Patent 5154926. October 13, 1992.
16. Swarbrick J, Boylan JC. Encyclopedia of pharmaceutical technology. vol 7. New York: Marcel Dekker, Inc; 1992; p. 101-139.
17. Harris MR, Ghebre-Sellassie I. Aqueous polymeric coating for modified release oral dosage forms. In: McGinity JW, editor. Aqueous polymeric coating for pharmaceutical dosage forms. 2nd ed. New York, NY: Marcel Dekker, Inc; 1997. p. 81-100.
18. Fekete R, Zelko R, Marton S, Racz I. Effect of the formulation parameters on the characteristics of pellets. Drug Dev Ind Pharm 1998; 24:1073–1076.
19. Gandhi R, Kaul CL, Panchagnula R. Extrusion and spheronization in the development of oral controlled-release dosage forms. Pharm Sci Technol Today 1999; 2(4):160-170.
20. Rouseff RL, Matthews RF. Nomilin, taste threshold and relative bitterness. J Food Sci 1984; 49:777–779.
21. Scholl FM, Munch JC. Taste tests. IV. Relative bitterness. J Am Pharmaceut Assoc, 1937; 26(2): 127–129.

TABLE 1: COMPOSITION OF FORMULATIONS (%W/W) OF BROMHEXIN HYDROCHLORIDE AND SALBUTAMOL SULPHATE

Ingredients	Formulations											
	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
Pellet Composition												
BMH*	20	20	20	20	20	20	-	-	-	-	-	-
SS*	-	-	-	-	-	-	20	20	20	20	20	20
MCC*	45	44	42	45	44	42	45	44	42	45	44	42
Lactose*	30	30	30	30	30	30	30	30	30	30	30	30
PVP*	3	3	3	3	3	3	3	3	3	3	3	3
Coating Composition												
BW#	2	3	5	-	-	-	2	3	5	-	-	-
CA#	-	-	-	2	3	5		-	-	2	3	5

* Used for preparation of pellets by extrusion spheronization
BMH: Bromhexine hydrochloride; SS: Salbutamol sulphate
Calculated on w/w basis of total pellets weight coated

TABLE 2: EVALUATION OF HOT MELT COATED PELLETS

Formulations	Friability %	Hardness kg/cm^2	Angle of repose	Bulk density g/cm^3	Tap density g/cm^3	Hausner Ratio	Carr's Index	Mean particle diameter µ	Drug content (%)
F1	0.19	1.77 ±0.25	22.55 ±1.16	0.777	0.849	1.093	8.48	825 - 882	98.6 ±0.7
F2	0.10	1.50 ±0.10	22.97 ±2.31	0.815	0.899	1.103	9.34	856 - 893	99.2 ±1.1
F3	0.25	1.77 ±0.12	22.53 ±2.20	0.807	0.913	1.131	11.61	871 - 911	100.5 ±0.8
F4	0.17	1.40 ±0.20	23.38 ±1.25	0.838	0.926	1.105	9.50	879 - 938	99.4 ±0.9
F5	0.26	1.87 ±0.35	22.97 ±2.24	0.803	0.932	1.161	13.84	894 - 939	98.9 ±1.1
F6	0.11	1.53 ±0.25	24.58 ±1.39	0.828	0.964	1.164	14.11	908 - 967	99.6 ±0.5
F7	0.23	1.67 ±0.25	23.07 ±3.49	0.824	0.887	1.076	7.10	827 - 876	101.1 ±0.4
F8	0.20	1.30 ±0.10	23.68 ±2.23	0.811	0.893	1.101	9.18	886 - 949	98.8 ±0.9
F9	0.27	1.70 ±0.17	24.31 ±1.54	0.794	0.911	1.147	12.84	896 - 936	99.3±0.8
F10	0.16	1.67 ±0.25	22.12 ±1.36	0.818	0.937	1.145	12.70	915 -955	99.7 ±1.3
F11	0.08	1.40 ±0.10	22.22 ±2.36	0.787	0.896	1.139	12.17	904 - 995	97.6 ±0.7
F12	0.14	1.63 ±0.12	21.93 ±1.40	0.858	0.973	1.134	11.82	938 - 989	99.2±0.9

TABLE 3: TASTE EVALUATION OF COATED PELLETS

Coated formulations	Sensory taste evaluation			
	0%	2%	3%	5%
Bromhexin + Bees wax	+++	++	+	-
Bromhexin + Cetyl alcohol	+++	++	+	-
Solbutamol + Bees wax	+++	++	+	-
Solbutamol + Cetyl alcohol	+++	++	+	-

- No bitter taste, + slightly bitter taste, ++ very bitter taste, +++ intensely bitter taste

Table 4: Taste evaluation study of hot melt coated pellets

Pellets formulations	Volunteers									
	V1	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**	**V10**
Uncoated pellets	+++	+++	+++	+++	+++	+++	+++	+++	+++	+++
F1	+	++	+	+	+	+	++	+	+	+
F2	0	0	0	0	0	0	+	0	0	0
F3	0	0	0	0	0	0	0	0	0	0
F4	+	+	+	++	++	+	0	+	+	0
F5	0	0	0	+	0	0	0	0	0	+
F6	0	0	0	0	0	0	0	0	0	0
F7	+	+	++	++	+	+	+	+	+	+
F8	0	0	+	0	+	0	0	0	0	0
F9	0	0	0	0	0	0	0	0	0	0
F10	+	+	+	++	+	++	+	+	+	+
F11	0	0	0	0	+	+	0	0	0	0
F12	0	0	0	0	0	0	0	0	0	0

*Bitterness scale: +++ = Very bitter; ++ = Bitter; + = Slightly bitter; 0 = No bitter taste

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