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Formulation and Evaluation of Taste Masked Tablet of Sodium Feredetate: Taste Masking Approach

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Abstract

Iron deficiency is the most common cause of anemia worldwide. In India, 30

Index terms— sodium feredetate, chewable tablet, taste masking, ?-cyclodextrin, electronic tongue.

1 Introduction

ron deficiency is the most common cause of anemia worldwide. In India, 30% adult males, 45% adult females, 80% pregnant females and 60% children Have iron deficiency. In our country important causes include poor dietary intake and bioavailability (most common), increased requirement during pregnancy, lactation and growth spurt, blood loss due to menstrual disorders and hook worm infestation. So, oral supplementation with iron preparations is frequently required [1][2]. The oral route of drugs administration is the most important method of administrating drugs for systematic effects. Except in case of insulin therapy, the parenteral route is not routinely used for selfadministration of medication. It is possible that at least 90% of all drugs used to produce systemic effects are administered by oral route. When a new is discovered, one of the first questions a pharmaceutical company asks is whether or not the drug can be effectively administered for its intended effect by oral route. If it cannot, the drug is primarily relegated to administration in a hospital setting or physician's office. If patient selfadministration cannot be achieved, the sales of the drug constitute only a small fraction of what the market would be otherwise [8][9][10] . These tablets are intended to disintegrate smoothly in mouth at a moderate rate either with or without actual chewing; characteristically chewable tablets have a smooth texture upon disintegration, are pleasant taste and leave no bitter or unpleasant taste [11] **??**12] . Taste is the ability to detect the flavor of substances like food, drugs etc. Taste is now becoming an important factor governing the patient compliance. It gained importance as the most of the drugs are administered through oral route. Administration of unpalatable drugs is hampered by their unpleasant taste particularly in case of pediatric and geriatrics. Various methods like coating, inclusion complexes, microen capsulation, granulation, adsorption, prod rug approach, addition of flavors and sweeteners, ion exchange resins are used for masking the taste of obnoxious drugs. However, there is no universal method for taste masking. Each method offers specific advantages and applications. One method is not suitable for taste masking all the obnoxious drugs. Several parameters like extent of bitter taste, dose, dosage form and type of the patient influence, the method to be used for masking the taste of the bitter drugs. Evaluation of taste masking by electronic tongue is a recent innovation. Advatab, Microcap, Liquitard, Kleptose, Formulplex and Formulcoat are the new I taste masking technologies, which are found to be better than existing ODT **??**13] .Cyclodextrin are cyclic (?-1, 4)-linked oligosaccharides of ?-D-glucopyranose, containing a relatively hydrophobic central cavity and hydrophilic outer surface. Owing to lack of free rotation about the bonds connecting the glucopyranose units, the cyclodextrin are not perfectly cylindrical molecules but the toroidal or cone shaped. Based on this architecture, the primary hydroxyl groups are located on the narrow side of the cone shape, while the secondary hydroxyl groups are located on the wider edge. During the past two decades, cyclodextrin and their derivatives have been of considerable interest in the pharmaceutical field because of their potential to form complexes with a variety of drug molecules. Cyclodextrin are used to increase the solubility of water insoluble drug through inclusion complexes formulation. The hydrophobic cavity of cyclodextrin is capable of trapping a variety of molecules within to produce inclusion complexes. Many advantages of drugs complex with cyclodextrin have been reported in scientific literature which includes-increased solubility,

enhanced bioavailability, improved stability, masking of bad test or odor, reduced volatility, transformation of liquid or gas into solid form reduced side effect, and the possibility of a drug release system etc **??**19] **??**20] **??**21] .

2 II.

3 Material and Methods

4 a) Material

Sodium Feredetate, ?-Cyclodextrin, Sodium Bicarbonate, Citric acid Anhydrous, Magnesium Stearate, Vanilla Flavour, Aspartame, Mannitol, Talc, Microcrystalline Cellulose (Avicel 102) was obtained as a gift sample from Pride drugs & Pharma (P)Ltd. Vodo dara, India, Lincoln pharmaceuticals Ltd. Ahemdabar, India. Other AR grade chemicals were purchased.

5 III. Preparation Inclusion Complexes a) Physical mixture or grinding method

Sodium Feredetate and ?-Cyclodextrin were accurately weighed in different molar ratios viz. 1:1, 1:2, 1:3 and 1:5 separately. Then it was mixed and blended thoroughly by triturating in a mortar for about 10 minutes. The powder mixtures were then pulverized through sieve no 80 and stored in desiccators till further use.

6 b) Kneading method

The inclusion complex of drug with ?-Cyclodextrin was prepared by wetting the physical mixture of Sodium Feredetate: ?-Cyclodextrin in the different molar ratios viz. 1:1, 1:2, and 1:3 in a mortar with water. Then kneaded the wet mixture thoroughly with a pestle to obtain a paste like consistency. The paste was then dried under vacuum at room temperature, pulverized by passing through sieve no 80 and stored in a desiccator till further use.

7 IV. Procedure of Evaluation of Taste by Electronic Tongue

The inclusion complexes were dissolved in purified water. All testing beakers contained 50ml of solution. When the reference electrode and sensors were dipped into a beaker containing a test solution, a potentiometric difference between each individually coated sensor with the Ag/Ag Cl reference electrode was measured and recorded by the E-Tongue software. Each sample was analyzed for 20sec. The liquid sensors and the reference electrode were then rinsed with purified water for 10sec after each sample analysis. Using well-conditioned sensors, each sample was usually tested five times by the rotation procedure.

8 V. Formulation of Chewable Tablet

Containing a Complex of Sodium a) Feredetate with ?-cyclodextrin i. Direct Compression Method Direct compression technique was used to formulate chewable tablet of Sodium Feredetate. Formulations compositions of chewable tablets are given in Table **??**.2 All raw materials used were passed through a sieve no. 60 prior to mixing. Prepared drug: ?-CD complex, sodium bicarbonate, citric acid, mannitol, MCC, was mixed for 15 minutes. Talc and magnesium stearate were added lastly before compression and mixed properly. The final mixture, ready for compression was directly compressed into tablets using a singlepunch tablet machine equipped with 16 mm flat punch.

9 VI. Evaluation of Tablets a) Pre-compression parameters

Prior to the compression, the powder blends of various batches were evaluated for their bulk and tapped density and from these values compressibility index and Hausner's ratio were calculated. While the flow properties of the powder bled were accessed from the angle of repose. The evaluation parameters were studied before and after addition of lubricants to check and compare the inherent flow properties of powders.

10 Angle of repose (?)

The frictional forces in a loose powder or granules can be measured by the angle of repose. This is the maximum angle possible between the surface of a pile of powder or granules and the horizontal plane. Tan ? = h/r ? = tan-1 (h/r) Where, ? is the angle of repose H is the height R is the radius The granules were allowed to flow through the funnel fixed to a stand at definite height. The angle of repose was then calculated by measuring the height and radius of the heap of granules formed.

11 b) Bulk density and Tapped Density

Both loose bulk density (LBD) and tapped bulk density (TBD) were determined. The accurately weighed amount of sample taken in a 25ml measuring cylinder of Borosil measured/recorded the volume of packing and tapped

100 times on a plane hard wooden surface and tapped volume of packing recorded and LBD and TBD calculated by following formula:

12 ii. Uniformity of thickness

Three tablets were picked from each formulation randomly and thickness was measured individually. It is expressed in mm and standard deviation was also calculated. The tablet thickness was measured using dial-caliper iii.

13 Hardness test

Hardness indicates the ability of a tablet to withstand mechanical shocks while packaging, handling and transportation. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm 2 . Three tablets were randomly picked and analyzed for hardness. The mean and standard deviation values were calculated.

14 iv. Friability test

It is the phenomenon whereby tablet surfaces are damaged and/or show evidence of lamination or breakage when subjected to mechanical shock or attrition. The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed (Initial) and transferred into friabilator. The friabilator was operated at 25 rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (Final). The % friability was then calculated by,

15 Percentage friability = Initial weight

Initial weight -Final weight × 100 v. Weight variation test Ten tablets were selected randomly from each batch and weighed individually to check for weight variation. U.S. Pharmacopoeia allows a little variation in the weight of a tablet. The following percentage deviation in weight variation is allowed.

vi. Drug content uniformity Three tablets were randomly sampled from each formulation batch, finely powdered and individually estimated for the drug content after suitable dilution, using UV-Visible spectrophotometer at 511.2nm after suitable dilution with distilled water or 0.1N HCL. Mean percentage drug content was calculated as an average of three determinations.

16 vii. In vitro disintegration time

The process of breakdown of a tablet into smaller particles is called as disintegration. The in vitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications. Disintegration test was carried out by using Disintegration test apparatus. One tablet is placed in each tube, and the basket rack was positioned in a 1litre beaker of water, at 37°C ±2°C. A standard motordriven device is used to move the basket assembly containing the tablets up and down through a distance of 5 to 6cm at a frequency of 28 to 32 cycles per minutes. The time taken for the tablet to disintegrate completely was noted.

17 viii. In Vitro Dissolution Studies

The in vitro drug release studies were performed using USP dissolution apparatus Type II (paddle) using 900ml of 0.1N hydrochloric acid as the dissolution medium. The temperature of the dissolution medium was maintained at 37±0.5 o C and the paddle was rotated at 50 rpm. Aliquots were withdrawn at different time intervals of 5,10,15,25 and 35,45 minutes and replaced by adding equal volume of fresh dissolution medium. The samples were suitably diluted and absorbance of the solutions was determined at the wavelengths 511.2nm in a UV-visible spectrophotometer.

18 VII. Result & Discussion

19 a) Characterization of Sodium Feredetate Inclusion Complex

i. Drug content estimation

Inclusion complexes of sodium feredetate with ?-CD were prepared by physical mixture, and kneading method. The results are shown in the Table **??**. The percentage drug content for all the prepared complex were found to be in the range of 97.76 ± 0.43 to 99.65 ± 0.32indicating uniform drug distribution.

ii.

20 Result of Taste Masking by Electronic Tongue

The metallic taste of the Sodium Feredetate was masked by kneading method in ratio of 1:2 (drug: ?-CD). The effect of a sweetener Aspartame, on masking Sodium Feredetate metallic taste was evaluated by e-Tongue and a PCA map was configured to determine the system discrimination power between the samples using the data generated (Figure 1 & 2). Sample 1-4 consist of pure drug, Sample 5-8 consist of 1:1 ratio of drug:?-CD, Sample

9-12 consist of 1:2 ratio of drug:?-CD, Sample 13-16 consist of 1:3 ratio of drug:?-CD, it shows that the Electric potential was decreases with decreasing the metallic taste of the drug.

21 VIII. Evaluation Parameters for

Chewable Tablets of Sodium Feredetate: ?-CD

22 a) Pre-compression Parameters Angle of repose (?)

Table **??** shows the results obtained for angle of repose of all the formulations. The values were found to be in the range of 30 0 .00' to 32 0 .93'. All formulations showed the angle of repose within 32 0 , which indicates a good flow property of the blend.

23 b) Bulk density and tapped density

Both loose bulk density (LBD) and tapped bulk density results are shown in Table **??**. The loose bulk density and tapped bulk density for all the formulations varied from 0.50 gm/cm3 to 0.57gm/cm 3 and 0.59 gm/cm3 to 0.65 gm/cm3 respectively. The values obtained lies within the acceptable range and not large differences found between loose bulk density and tapped bulk density. This result helps in calculating the % compressibility of the powder.

24 c) Hausner's ratio

Table **??**, shows the result obtained for Hausner's ratio of all formulations. The values were found to be in the range of 1.15 -1.19. All formulations showed the Hausner's ratio within the range, which indicates a good flow property of the granules.

25 d) Percentage compressibility

This percent compressibility of powder mix was determined by Carr's compressibility index. Table **??**, shows the results obtained for percentage compressibility. The percent compressibility for all the nine formulations lies within the range of 12.88to 20.00. All formulations are showing good compressibility.

26 IX. Post Compression Parameters a) Post-compression parameters

All the tablet formulations were subjected for evaluation according to various official specifications and other parameters. Shape, thickness, hardness, friability, weight variation, in vitro disintegration time, drug content, in vitro dissolution studies.

27 b) Shape and color of tablets

Randomly picked tablets from each formulation batch examined under lens for shape and in presence of light for color. All tablets of all the batches showed flat, circular in shape and pale yellowish in color.

28 c) Uniformity of thickness

The thickness of the tablets was measured by using dial caliper by picking the tablets randomly. The mean values are shown in Table **??**. The values are almost uniform in all formulations. Thickness was found in the range of 2.43 mm to 2.62 mm respectively.

29 d) Hardness test

Table **??**, shows results of hardness. Hardness test was performed by Monsanto hardness tester. Hardness was found to be within 5.13kg/cm 2 to 7.00 kg/cm 2 as these tablets are chewable tablet. The lower standard deviation values indicated that the hardness of all the formulations were almost uniform inspecific method and possess good mechanical strength with sufficient hardness.

30 e) Friability test

The study results are tabulated in Table **??**, was found well within the approved range (<1%) in all the formulations. Formulation F1 to F9 possesses good mechanical strength.

31 f) Weight variation test

The percentage weight variation for all the formulation is tabulated in Table **??**. All the tablets passed weight variation test as the % weight variation was within the pharmacy opoeial limits of ± 10 %. It was found to be from 950.33 to 1199.66mg. The weight of all the tablets was found to be uniform.

g) Drug content uniformity

Three tablets were randomly sampled from each formulation batch, finely powdered and individually estimated for the drug content after suitable dilution, using UV-Visible spectrophotometer at 511.2nm after suitable dilution with distilled water or 0.1N HCL mean percentage drug content was calculated as an average of three determinations.

h) In vitro dissolution studies

In vitro drug dissolution studies were carried out using Electro Lab dissolution tester USP type II (Model TDT 06PS).

i) Method

Dissolution medium: 0.1N HCL solution Dissolution volume: 900mL RPM : 50 RPM Temperature : 37 0 ± 0.5 0 Samples withdrawn: 5, 10, 15,20,30,40 mins

The formulation F1, F2 & F3 the concentration of mannitol was less & showed improper hardness with % in vitro drug release up to 80% in 40 mins (Table **??**& Figure **??**). But with a view to get better table ting properties further formulation was prepared with addition of MCC.

In formulation F4, F5 & F6 (Table **??**& Figure **??**), MCC was added in same concentration and mannitol in different concentration, the result showed better hardness and better drug release but the disintegrating time of tablet was less and such a large amount of powder leads to inconvenient thus further formulation was developed with higher concentration of mannitol by omitting MCC.

In formulation F7, F8 & F9 (Table 8& Figure **??**), mannitol concentration was increased and that formulations showed better hardness, good % in vitro drug release and disintegration time was increased up to the limit. From these formulations F8 had shown better properties.

X. Conclusion

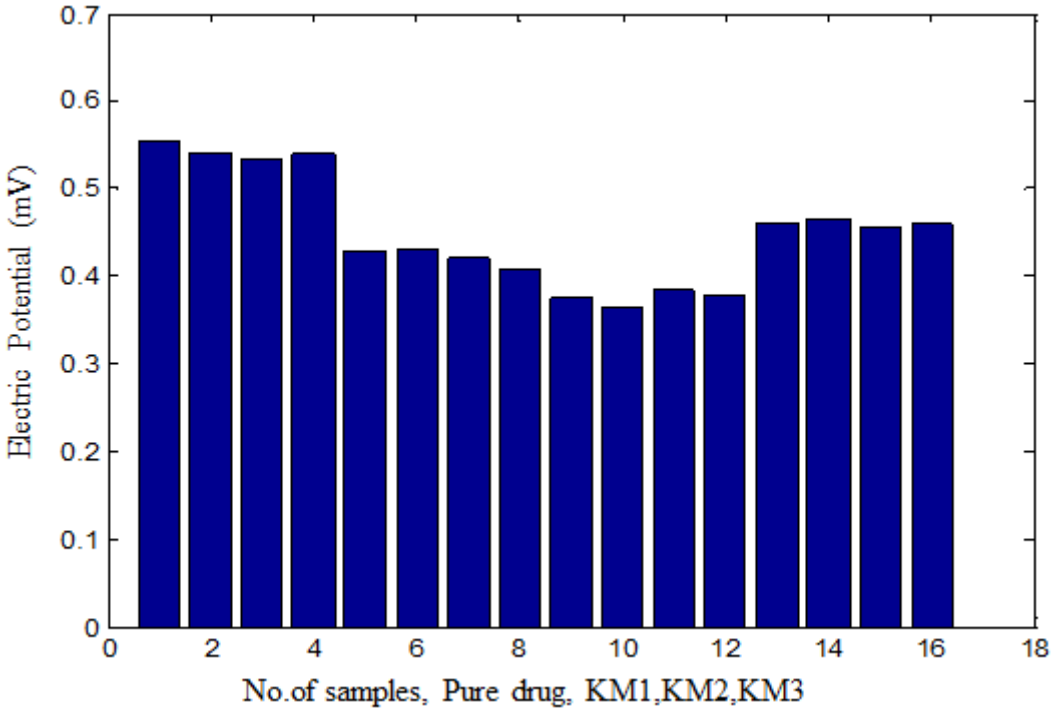
In the present study attempt has to mask the metallic taste of Sodium Feredetate. Taste masking has been carried out by using two different method i.e. physical mixture and kneading method, it was found that the metallic taste of the drug masked by kneading method in ratio of 1:2 (drug:?-CD). The evaluation of taste was performed by E-tongue on the basis of electronic potential. Fizzy chewable tablets containing Sodium Feredetate was successfully formulated using suitable excipients to delivery drug via oral route. Further, by varying in amount of sweetener, binder and super disinter grant, nine formulations were prepared and coded as F1-F9. All the formulation has shown both pre-compression and post-compression characters within acceptable limits. The chewable tablets were prepared by the method of direct compression using16 mm curved flat punches.

XI.

Summary

The use of conventional oral tablets may pose major problem due to large dose size and decreased patient compliance. Therefore, to overcome this drawback, chewable tablets were prepared with suitable sweetener, flavor for better patient acceptance. Apart from that chewable tablets have an added advantage that effectiveness of the therapeutic agent is improved by the reduction in size that occurs during mastication of the tablet before swallowing and also better bioavailability through by-passing disintegration. In the present work an attempt was made to design a chewable tablet containing Sodium Feredetate with suitable excipients for the treatment of iron deficiency anemia. The objective of the present research work was to select suitable excipients, which should show good pre-compression and post-compression parameters, and also chewable tablets with good acceptable property like flavor, taste and mouth feel. The drug is having metallic taste so taste masking of drug becomes an important step prior to formulating these drugs into an oral dosage form. Hence the aim of the project is to enhance and mask the taste of drugs and formulate them into an orally chewable tablet. So, with a view to enhanced the patient compliance, and provide a quick onset of action, May increase the solubility and masking its metallic taste. Among the various inclusion complexes prepared, formulation i.e., the inclusion complex of sodium Feredetate with ?-CD (1:2 molar ratio) prepared by kneading method shows good dissolution rate. So, it was decided to use to formulate fizzy chewable tablets .Further, preliminary work for selection of suitable excipients was done and a final formula was developed with acceptable precompression and post-compression evaluation parameters.

Figure 1:



1

Figure 2: Figure 1 :

2

Figure 3: Figure 2 :

8

		% CDR	
TIME (mins)	F7	F8	F9
0	0	0	0
5	31.72	35.35	38.30
10	48.97	57.53	60.76
15	55.49	72.52	73.27
20	66.76	79.74	81.51
30	72.35	87.73	87.51
40	89.60	96.33	93.81

Figure 4: Table 8 :

[Brittenham et al. ()] , G Brittenham , R Hoffman , E J Benz , L E Silberstein , H E Heslop , J I Weitz . *Hematology: Basic Principles and Practice* 2012. (6th edition)

[Abdel et al. ()] 'Chewable Tablets: Is this Dosage Form Well Evaluated by Palestinian Health Professionals'. N Abdel , O Abeer , A Ghosh , Al-Jabi S Jaradat , N . *The Islamic University* Journal2007.

[Ramakrishnan and Yip] 'Experiences and challenges in industrialized countries:Control of iron deficiency in industrialized countries'. U Ramakrishnan , R Yip . *J Nutr2002* p. .

[Debjit and Chiranjib ()] 'Fast Dissolving Tablet: An Overview'. B Debjit , B Chiranjib , Krishnakanth , MargretC . *Journal of Chemical and Pharmaceutical* Research2009. 1 (1) p. .

[Patil and Vishwajith ()] 'Formulation Development and evaluation of chewable tablets containing non-sedating Antihistamin'. J Patil , V Vishwajith , GopalV . *Journal of Pharmaceutical and Scientific Innovation* 2012.

[Mehta ()] 'Iron deficiency anemia'. B C Mehta . *Shah SN, API Textbook of Medicine. 7 th ed. Mumbai, the Association of Physicians of India*, 2003. p. .

[Lachmann et al.] *Pharmaceutical Dosage Forms: Tablets*, Leon Lachmann , A Herbert , Joseph B Liberman , Schwartz . 1989. (2nd edition)

[Lachman et al. ()] *The Theory and Practice of Industrial Pharmacy*, L Lachman , H A Lieberman , J L Kanig . 1987. p. . (Third Indian edition)