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PREPARATION AND EVALUATION OF PARACETAMOL TABLET

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ABSTRACT

Tablets are the medicament with suitable excipients. It comprises a mixture of active substances and excipients, usually pressed or compacted from a powder into a solid dose. Paracetamol, also known as acetaminophen, is a painkiller that is popular throughout the world because it does not irritate the stomach. Paracetamol was first discovered to have both analgesic and antipyretic properties in the late nineteenth century. The aim of present work was to Formulate, develop and evaluate paracetamol tablets. In evaluation of paracetamol tablets we were performing determination of different parameters like weight variation, friability, hardness, drug content, identification test, disintegration time and dissolution profile. By performing weight variation and friability test we were fond that tablet show acceptable value. The formulated tablets thereafter were evaluated for the characterization for granules to check such as flow property, bulk density, tap density etc.

KEYWORDS: Tablets, Paracetamol, Acetaminophen, Evaluation, Disintegration time.

INTRODUCTION

Tablets are the solid oral dosage forms formulated with their greatest dose precision, low-cost, easy transportation and patient compliance and that's why more than 70% of drug dosage forms are formulated in tablets. Binder plays an important role in formulation of tablet dosage form. It may be added either dry or in solution form to the tablets prepared by wet granulation.[1,2] It help the powder to turn into granules which possesses good flow properties and compact ability and enhances cohesiveness. Quality of tablet depends on type, quantity and the way the binder is added. Therefore, choice of binder is extremely important in determining final tablet performance. Tablets are solid masses made by the compaction of

suitably prepared medicament (granules) by means of tablet machine.[3] The clinical effectiveness exerted by tablet formulation depends on two factor such as, labeled amount and its availability to the body. The main objective of oral tablet is to deliver the drug to human body at certain amount through gastro intestinal system for producing therapeutic effect. Excipients are the substance formulated alongside the active ingredient of medication, included for the purpose of long term stabilization, bulking up solid formulation that contain potent active ingredients in small amount such as lubricants, binders, disintegrants etc. Excipients can have multiple dosesin a single dosage form or even in various roles in different formulation types.[4] Various different examples of binders used in tablets are cellulose, gelatin, polyvinyl pyrrolidone, starch, sucrose, mannitol, polyethylene glycol and liquid glucose, etc. Coconut oil is a white solid highly saturated fat with a characteristic odor. It is extracted by either cold pressing or solvent extraction of the coconut flesh. Chemically it is very high in saturated fats, typically up to 85%. When the solid is further treated by fractionating it gives clearoil. This commercial product is referred toas fractionated coconut oil. It contains more fatty acids of a shorter chain length, like octanic (8 carbon atoms) and decanoic (10 carbon atoms) than the solid.[5] Paracetamol (INN)) or acetaminophen (USAN) is a widely-used analgesic and antipyretic medication. Derived from coal tar, it is the active metabolite of phenacetin, but unlike phenacetin, paracetamol has not been shown to be carcinogenic in any way. Paracetamol generally is well tolerated, lacks many of the side-effects of aspirin, and is available over-the-counter. It is commonly used for the relief of fever, headaches, and other minor aches and pains. In combination with non-steroidal anti-inflammatory drugs (NSAIDs) or opioid analgesics, paracetamol is used also in the management of more severe pain. Paracetamol is a major ingredient in numerous cold and flu remedies. While generally safe for human use at recommended doses, acute overdoses of paracetamol can cause potentially fatal liver damage and, in rare individuals, a normal dose can do the same. Paracetamol toxicity is the foremost cause of acute liver failure in the Western world, and accounts for most drug overdoses in the United States, the United Kingdom, Australia and New Zealand. This risk is heightened by alcoholism. A 2008 study indicates that Paracetamol given to infants may also be linked to an increased risk of developing asthma in children.[7-10]

Experimental

Materials

Paracetamol was obtained as a gift sample from Macleods Pharmaceuticals, Mumbai. HPMC

K4M, HPMC K 15 M was purchased from Himedia Laboratory, Mumbai. Xmnthan gum, Guar gum purchased from CDH chemical Pvt. Ltd. New Delhi. Dialysis membrane of Mol Wt cutoff 1200 was purchased from Himedia Laboratory, Mumbai. Demineralized and double distilled water was prepared freshly and used whenever required. All other reagents and chemicals used were of analytical grade.

Preformulation studies

Melting point

A small quantity of powder was placed into a fusion tube. That tube was placed in the melting point determining apparatus (Chemline) containing castor oil. The temperature of the castor oil was gradual increased automatically and read the temperature at which powder started to melt and the temperature when all the powder gets melted.

Solubility

Solubility of the drug was determined by taking some quantity of drug (about 1-2 mg) in the test tube separately and added the 5 ml of the solvent (water, ethanol, methanol, 0.1N HCL, 0.1N NaOH, chloroform and 7.4 pH buffer) Shake vigorously and kept for some time. Note the solubility of the drug in various solvents (at room temperature).

Physical characteristics

By visual examination, the drug was identified for physical characters like colour, texture, odour etc.

Compatibility study

Compatibility studies were performed using IR spectrophotometer. the IR spectrum of pure drug and physical mixture of drug and polymer is studied. The peaks obtained in the spectra of each formulation correlates with the peaks of drug spectrum. this indicates that the drug was compatible with the formulation components.

Preparation of tablets

Weigh 1.0 g of 4-aminophenol into a 50 cm^3 conical flask. Add 9 cm^3 of distilled water and shake the mixture briskly to suspend the solid in water. In a fume cupboard, add 1.1 cm^3 (1.17 g) of ethanoic anhydride to the stirred suspension and gently shake to mix. The solid will dissolve after about 30 seconds. Continue shaking and a precipitate will form after 2 minutes. After 10 minutes filter the solid off under suction filtration, wash with a little cold

water and dry. Note: Use a Buchner flask and funnel connected to a vacuum pump (water pump). Clamp the flask to keep it stable. Put a filter paper in the funnel, attach the flask to the pump and pour through about 10 cm^3 water as a practice run and to wet the filter paper. Remove the vacuum tube, pour out the water and then do the real filtration. If you do not manage to transfer all the solid from the reaction mixture into the funnel at the first attempt just pour the filtrate back into the conical flask and repeat the process. Remove a small sample (A), dissolve in minimum quantity of ethyl ethanoate and keep in a labelled sample tube. To recrystallize the sample put it into a small conical flask. Dissolve the crude product in the minimum volume (probably about 15 cm^3) of distilled water at 80 °C. Heat it in a hot water bath (80 °C) until the solid dissolves. Add a few extra drops of hot water if necessary to dissolve the solid. Cool the solution under a tap or preferably in ice. Collect the recrystallized product by suction filtration, washing with 5 cm^3 of ice-cold distilled water. Dry the recrystallized product between filter papers and then in an oven (about 105 °C) and determine the yield. Calculate the percentage yield. Remove a small sample (B), dissolve in minimum quantity of ethyl ethanoate and keep in a labelled sample tube. Find the melting point of the dry, recrystallized product. The melting point of pure paracetamol is 169-171^oC. Now run a thin layer chromatogram using the method in *Microscale investigation of paracetamol synthesis*. Run the crude paracetamol (A) and recrystallized paracetamol (B) against (a) 4-aminophenol, (b) pure paracetamol and (c) a mixture of 4-aminophenol and paracetamol (all dissolved in ethyl ethanoate).

RESULTS AND DISCUSSIONS

Physical properties of paracetamol and Mucoadhesive polymers like bulk density, tapped density, % compressibility and Hausner ration results shown in Table 1. Tablets are required to be packed in standard Aluminum Strip /Aluminum Blister. The aluminum strip should be of thickness not less than 0.04mm confirming to IS- 8970:1991. The packing material should have compatibility with the tablets. Blister/Aluminum strip pack of not more than 140 tabs should be packed in thick cardboard box so that container should provide adequate protection to the drugs. The hardness of tablets of each batch ranged between 4.5 to 6.8 kg/cm^2 this ensures good handling characteristics for all batches. The packing shall be sufficient to withstand, without limitation, sunlight, humidity, salt and precipitation during transit and storage. Packing case size and weights shall take into consideration, wherever applicable, the remoteness of goods final destination. All primary packing containers which come in contact with Pharmaceuticals or drug content shall strictly confirm to the specification in the relevant

Pharmaceuticals to protect the quality and integrity of goods. It was performed using usp disintegration device. 6 tablets were Placed in disintegration test apparatus. It was maintained at 37 ±0.2c containing distilled water. The time taken for a tablet to disintegrate was noted down. For this test u.s.p. Type- 1 (basket) apparatus was used. phosphate buffer (ph 5.8) as dissolution medium: the tablets were immersed into 900 ml. Of dissolution medium, the Temperature of the dissolution medium was maintained at 37± 0.2c. The basket was rotated at a speed of 50 rpm. At 5, 10,20,30,45,60 minutes 1 ml. Of the medium was pipette out and replaced with fresh medium (phosphate buffer ph 5.8). This was continued all along for 1 hour. The pipetted out samples were then diluted to 10 ml. With fresh dissolution medium and were then filtered. The absorbance of the filtered samples was determined Using u.v. Spectrophotometer at λmax 243 nm. Paracetamol in combination with hydrochlorothiazide was not mutagenic in the Ames microbial mutagen test with or without metabolic activation. Swelling study was performed for all the batches (F1 to F9) up to 8 hr. the results of swelling index From the above results it was conclude that swelling increases as the time proceeds because the polymer gradually absorb water due to hydrophilicity of polymer. In the present study, the higher selling index was found for tablets of batch F9 containing HPMC K15M having nominal viscosity of 15.000 cps. Thus, the viscosity of the polymer had major influence on swelling process, matrix integrity, as well as adhesion capability, hence form the above result it can be concluded that linear relationship exists between swelling process and viscosity of polymer. A pre-weighed tablet with a tablet holder was placed in the medium, and the weight of the swollen tablet was noted at predefined time intervals. The swelling index was calculated by the following equation: swelling index = (W t - W 0)/W0, where W 0 and Wt are the initial weight of tablet and weight at time t respectively. Stability studies of the optimized formulations were performed at room temperature, at 40^0a and 4^0C a period up to 30 days. The sample were withdrawn after periods of 30 days and were analyzed for its appearance, hardness, friability, drug content and in vitro release. . the results revealed the no significant changes in appearance, mucoadhesive strength and invitor release for F1 to F9 formulations When it stored at the three storage condition. However there was slight variation in invitro release for when it is stored at rom temperature and 40^0C.

Table 1: Physical parameters of polymers.

Polymers	Bulk Density (gm/cm3)	Tapped Density (gm/cm3)	Compressibility Index	Hausner Ration
HPMC K4M	0.36	0.46	21.96	1.28
HPMC K 15 M	0.33	0.39	15.56	1.43
Xmnthan gum	.37	0.5	25.0	1.33
Guar gum	0.35	0.49	20.60	1.45

CONCLUSION

The tablets were successfully formulated and evaluated. The prepared Paracetamol granules were evaluated for angle of repose, bulk density, tapped density, Hausner's ratio and Carr's ratio and the results of the parameters of tablets with starch binder was found to be better in Angle of repose, where as tablets with acacia binder showed good flow ability and was superior in Hausner's ratio, Carr's index. The results of all the tests were found to be with in the limits. In the evaluation tests, tablets with starch binder passed in disintegration, dissolution, weight variation, thickness and diameter, friability and hardness tests where as tablets with acacia binder passed weight variation, thickness and diameter, friability and hardness tests but did not pass disintegration and dissolution tests. In vitro dissolution studies, around 94.62% of the drug was released with in 30 minutes for tablets with starch binder while only 33.98% of the drug was released within30 minutes for tablets with acacia binder. Hence, according to our study, starch paste better binder thana cacia paste in the preparation of paracetamol tablets.

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