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Research Article

FORMULATION AND EVALUATION OF DEXTROMETHORPHAN HYDROBROMIDE SOFT GELATIN CAPSULES

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ABSTRACT

The present study provides a new composition for treating cough, comprising dextromethorphan HBr . In the present work the soft gelatin capsules were formulated comprising 15mg dextromethorphan HBr using PEG 400, PG , PVP k-30 and purified water. The prepared soft gelatin capsules were evaluated for weight variation test, assay, dissolution and disintegration. The capsules had a fill weight of 400 ± 5%, Disintegration time of 8-10 minutes and showed 97.00% to 99.50% of labelled amount of dextromethorphan HBr indicating uniformity in drug contents. The capsules containing 335 mg/capsule of propylene glycol released 100.07% of dextromethorphan HBr at the end of 9 minutes. Thus, it may be concluded that soft gelatin capsules of dextromethorphan HBr could be successfully prepared with existing technology and machinery which have a commercial viability and enhance patient compliance with improved bioavailability.

Keywords: *capsule, soft gelatin, Dextromethorphan HBr*

INTRODUCTION:

Soft gelatin capsules are the formulations which are formed, filled and sealed in one continuous operation[1]. Softgels offer several advantages like versatile size, shape and elegance, tamper proof, content uniformity etc. Several advantages of soft gelatin capsules derive from the fact that these contain the active ingredient in solution, suspension or emulsion.

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This will inherently lead to better absorption of the active ingredient as compared with delivery of a tablet or a powder and patients find it easier to swallow capsules than tablets. This preference has promoted pharmaceutical manufactures to market the product in capsule form[1-3]. The present invention provides a new composition for treating cough, comprising dextromethorphan HBr. Soft gelatin capsules shell was prepared using gelatin and glycerine as plasticizer. Capsules fill solution was prepared by using antitussive drug dextromethorphan HBr and was dissolved in hydrophilic solvent PEG 400[5].

MATERIALS AND METHODS

Dextromethorphan HBr USP, polyethylene glycol (PEG) 400, propylene glycol, PVP K-30 were obtained as gift sample from onerioe

chemicals Ltd, saibaba surfactants pvt ltd, vision chemicals respectively. All the chemicals and reagents used in the study were of analytical grade.

Preparation of Fill Solution

Drug fill solution was prepared by accurately weighing required quantities of dextromethorphan HBr along with various excipients as shown in Table 1. PEG 400 and PG was collected into a preheated jacketed vessel. Providone was added to this mixture and homegenized till to get a clear solution. Dextromethorphan HBr is now added to it and clear solution is obtained by stirring. Finally purified water is mixed and blend is cooled to 25°C [6-9].

Table 1: Composition of Soft Gelatin Capsules (Quantities/capsules in mg)

Sr.No	*INGREDIENTS(mg)*	*F1*	*F2*	*F3*	*F4*	*F5*
1	*Dextromethorphan HBr*	*15*	*15*	*15*	*15*	*15*
2	*PEG- 400*	*329*	*385*	*307*	*314*	*335*
3	*Propylene glycol*	*24*	*-*	*40*	*35*	*20*
4	*PVP K-30*	*12*	*-*	*20*	*20*	*20*
5	*Purified water*	*20*	*-*	*17*	*15*	*10*

Preparation of Gelatin Shell

Gelatin shell was prepared using glycerine (12%), gelatin (45%), sorbitol (6%) and purified water (40%). Glycerine along with purified Water and sorbitol was mixed in shell preparation vessel by vacuum and the mixture was then heated to a temperature of 80°C. Once temperature was achieved, gelatin loaded into the shell preparation vessel by vacuum and completely mixed to get a uniform mixture. Vacuum was applied to remove air bubbles from the gelatin paste. Gelatin paste was then unloaded into preheated gelatin tanks maintained at 57°C to 60°C during the encapsulation process[8-12].

Encapsulation

Encapsulation of fill solution into gelatin paste was done using rotary die machine. migli oil 812 was used for machine lubrication. Capsules were dried for 48 hours at 30°C and 18% relative humidity. Washing of capsules was done using isopropyl alcohol to remove the adhering oil on to the capsules used for the purpose of lubrication during encapsulation. Washed capsules were then subjected to inspection manually for removal of physical rejects like damaged or improperly filled capsules, leaked capsules etc. [13-14].

EVALUATION OF DRUG

Organoleptic Properties

The drug was examined and identified from its Organoleptic properties like colour and odour. This was shown in table

Table 2. Organoleptic properties of drug

Sr. No	*TEST*	*DESCRIPTION*
1	*Colour*	*White*
2	*Odour*	*Faint odour*
3	*Appearance*	*Powder*

Infrared Spectroscopy

The IR spectrum of pure drug was found to be similar to standard spectrum of Dextromethorphan HBr.

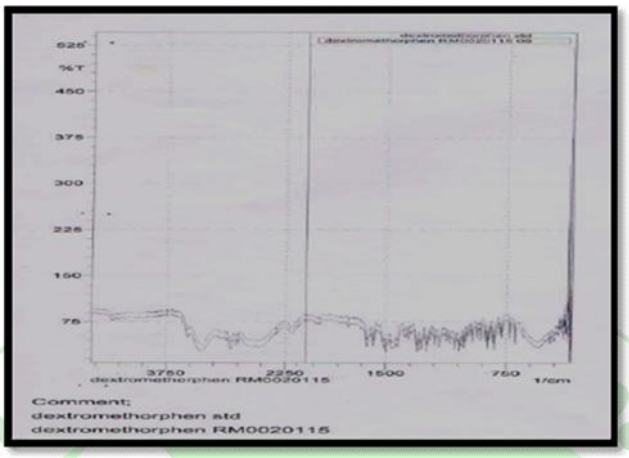


Fig 1. The IR spectrum of test and standard drug

Solubility Study

This study includes selection of suitable solvent to dissolve the pure drug as well as excepients used for the design of soft gelatine capsules.

The sample was quantitatively tested for its solubility in various solvents. It was determined by taking 1mg drug sample in necessary amount of solvent such as water, ethanol, chloroform, ether etc., in small test tube as well as solubilised by shaking, according to USP.

The drug sample was found Freely soluble in alcohol and in Chloroform; Sparingly soluble in water; insoluble in ether [15].

UV spectroscopy

Different aliquots of Dextromethorphan hydrobromide in range 1 - 9 ml were transferred into series of 10 ml volumetric flasks and the volume was made up to the mark with 0.1N HCL to get concentrations 10,20, 30, 40, 50, 60, 70,80 and 90 µg/ml, respectively. The solutions were scanned on spectrophotometer in the UV range 200 - 400 nm. The spectrum was recorded at 281 nm. The calibration plot was constructed as Absorbance vs concentration [24].

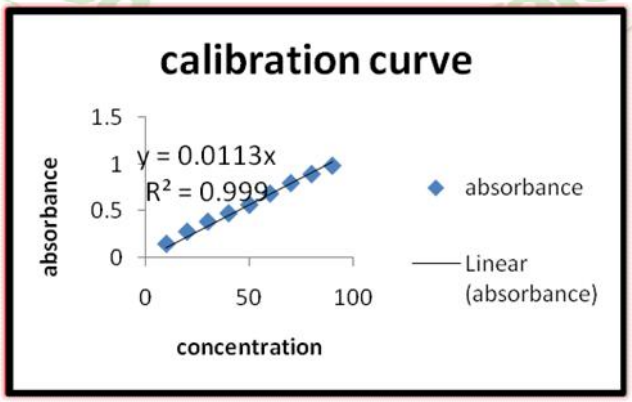


Fig 2: Calibration curve of Dextromethorphan HBr

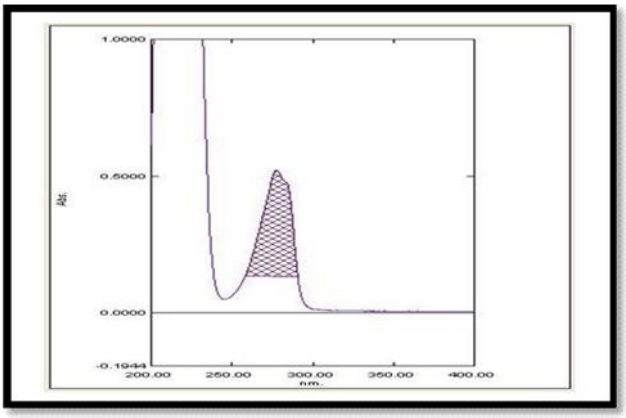


Fig 3: λ_{max} of Dextromethorphan HBr in 0.1N HCl

Ph- Dissolve 1 gm drug in 100 ml water and check pH by digital pH meter. The pH was found to be 5.5[24].

Melting point- The melting point was determined by capillary method using digital melting point apparatus. The capillary tube was fused and filled by pressing the open end gently into pure drug sample and packed by tapping the bottom of the capillary on a hard surface so that the drug packed down into the bottom of the tube. When the drug packed down into the bottom of the tube, the tube was placed into the slot of the apparatus, the apparatus was started and the temperature was noted at which the drug melt. This was performed thrice and the average value was calculated [24].

Table 3. Melting point range of Dextromethorphan HBr

Sr. No	*Reported Melting Point*[25]	*Observed Melting Point*	
1	*126°C*	*125.5°C*	*126°C ±0.3*
2		*125.7°C*	
3		*126.5°C*	

Moisture Content (water %) - Moisture content of drug is determined by using KF apparatus. Dry methanol is firstly used to neutralize the KF reagent and then weighed quantity of water is added to mixture of neutralized KF reagent. The water factor is displayed on screen. After that weighted quantity of API is added to it and the amount of KF consumed with % of water in sample is displayed on the screen. moisture content of drug was found to be 5.23% [24].

EVALUATION OF SOFT GELATIN CAPSULES

Appearance- 10 capsules from each formulation batch were taken and inspected visually for colour, shape, leakage etc.

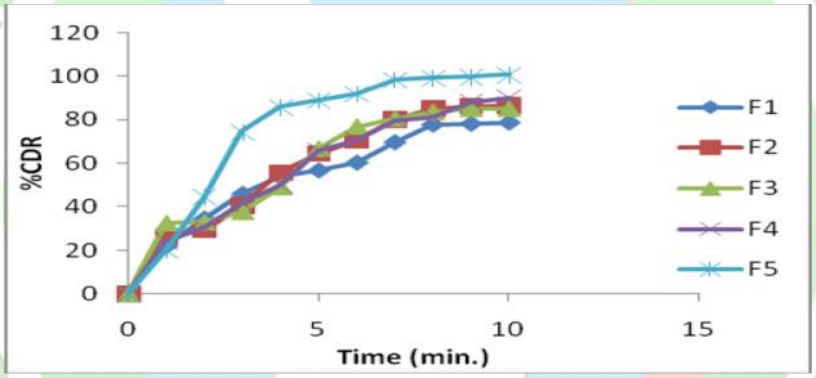
Disintegration Test- Disintegration test was performed by placing six capsules into the basket-rack assembly of the apparatus and discs were placed in each tube. The temperature of water inside the beaker was maintained at 37±5°C. Time in minutes was recorded at which last capsule of 6 capsules; disintegrate completely except fragments from the capsule shell [24].

Rheological Studies-Viscosity is one of the important parameters which provide vital information during the optimization of the liquid filling formulation for soft gels. In general, the viscosity of liquid filling formulations for soft gels is in the range of 0.222–3000cps [18].

pH -pH is one of the most important parameter involved in the liquid filling formulations. Soft gel formulation should have a pH range between 2.5 and 7.5. The developed formulations were evaluated for pH by and estimations were carried out in triplicate and shown in table 4 [19].

Assay- the assay was performed by transferring 10 soft gel capsules to the 1000 ml volumetric flask. Adding 900 ml of diluting solution, and sonicating for 60 minutes with occasional manual shaking. Cooling to room temperature, stirring for 60 minutes on a magnetic stirrer. Diluting to volume with diluting solution and mix well. Filter directly a portion of resulting solution with a 0.45 µm filter; discard the first 1 ml of the filtrate and use the remaining as a test solution. Finally the drug is assayed using HPLC at 281nm (mobile phase- 0.05 M Monobasic Potassium Phosphate buffer and methanol, column- Phenomenex Luna C18, 4.6 mm x 150 mm, flow rate – 1ml/min, injection volume- 10µl, run time- 25min) [24].

In vitro drug release-In vitro dissolution studies were conducted using 1000 mL of 0.1N HCl as a dissolution medium using a USP type II paddle method dissolution apparatus. A temperature of 37±5°C °C and a rotation speed of 100 rpm were maintained. A 5 mL sample was withdrawn at predetermined time intervals over a period of 2 hrs and then replaced with the same volume of fresh dissolution medium. The filtered samples were suitably diluted and analyzed at 280 nm using UV-visible spectrophotometer (UV-3000, shimadzu)[24].



Comparative *in-vitro* dissolution profiles for F1- F5

Table 4: Data obtained from Evaluation of Soft gelatin capsules.

Formulation code	***F1***	***F2***	***F3***	***F4***	***F5***
Visual inspection	*Red, drug get crystallized, oval , leakage*	*Red hazy, oval, leakage*	*Red, cloudy, deshaped, leakage*	*Red, hazy, deshaped*	*Red transparent oval*
pH	*5.6*	*5.6*	*5.4*	*5.9*	*5.5*
Average gross weight	*600mg±5%*	*600mg±5%*	*600mg±5%*	*600mg±5%*	*600mg±5%*
Average net weight	*400mg±3%*	*400mg±3%*	*400mg±5%*	*400mg±6%*	*400mg±7%*
Disintegration time	*12min*	*13min 44sec*	*9min 24 sec*	*9min 30sec*	*9min 16 sec*
Viscosity	*77.81*	*67*	*198*	*96.8*	*131*
Loss on drying	*8.2%W/W*	*9%W/W*	*9.4%W/W*	*13%W/W*	*8.6%W/W*
%assay	*99%*	*103%*	*98%*	*102%*	*103.3%*

CONCLUSION

The drug solvent, co solvent and solubilizer concentration was found to influence the release of drug from the formulation. As the concentration of solubilizer and co solvent is increased, drug release was also increased but viscosity also increases. The drug solvent, co solvent and solubilizer concentration was found to influence the visual characteristics of dosage form. F1 F2 F3 shows leakage of capsules because of high water content. F4 becomes hazy because peg 400 concentration is insufficient to dissolve drug. F1 drug gets re crystallized due to less amount of PVP K-30.

It was concluded that from overall comparison with parameters of all the formulations like disintegration time, appearance, viscosity, in vitro drug release formulation f5 found to be best optimized formulation. In conclusion it can be said that, the formulation F5 containing 335ml PEG400, 20ml PG , 20mg PVP K-30 and 20mg purified water show better drug release than other formulations. Formulation F5 apsules with 9.6min as disintegration time could be used to treat cough patients . Soft gelatin capsules of dextromethorphan HBr could be successfully prepared with existing technology and machinery which have a commercial viability and enhance patient compliance with improved drug accuracy and dose uniformity.

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