**Original Research Article**

**DEVELOPMENT AND CHARACTERIZATION OF PALONOSETRON HYDROCHLORIDE JELLIES**

**Abstract:**

Dysphasia is one of the most common diseasesmainly in geriatric and podiatric populations. As swallowing is the main difficulty in dysphagic patients, in that situation medicated jelly preparations are the best alternative to conventional doses forms (tablets and capsule doses form). Fast dissolution results in better absorption of the drug from medicated jellies ultimately better onset of action. This research article is aimed at the formulation and evaluation of palonosetron hydrochloride oral jelly.

Two methods i.e., congealing and heating were chosen to prepare sucrose-based jellies. All prepared formulation were evaluated on different parameters. All formulation was found free from any type of gritty particles. Out of all formulations MJ1 was found best formulation on the basis of drug release profile i.e., 79.22% within 30mins. Accelerated stability studies also confirmed that MJ1 and MJ2 are the best formulations. This study can be summarised that Palonosetron hydrochloride-loaded jellies may be present in mouth for more time with bypassing first-pass metabolism.

**Keywords:**Palonosetron hydrochloride, medicated jellies, Stability studies.

**Introduction:**

Patient compliance and easy dose administration are the two major concerns to be considered during drug dose development. Tablets and capsules are not a good choice for patients suffering from swallowing problems, especially in the geriatric and pediatric populations and dysphagic patients. Medicated jellies can provide ease of administration for such a population by overcoming the main problem1.

Medicated jelly development is the best alternative for dysphagic patients with a fast dissolution rate and rapid absorption of a drug resulting in better bioavailability. Jellies are prepared in the form of nongreasy semisolid solutions/suspensions which aretransparent or translucent in nature. In medicated jellies small to large organic particles are incorporated within the liquid outer layer. These can be administered without water or any type of liquid. Medicated jellies rapidly melt in the oral cavity at 37°C. The major limitation of jellies they get tough with time during storage. Attraction toward jelly is also a positive point for the podiatric population. During chewing medicated jelly rapidly releases drug which is rapidly absorbed through saliva and directly enters systemic circulation, bypassing first-pass metabolism2.

Palonosetron Hydrochloride is one of the most potent drugs to minimize “delayed chemotherapy-induced nausea and vomiting” one of the side effects of chemotherapy that occurs after more than 24 hours of therapy3. Palonosetron hydrochloride is administered intravenously or orally before a half hour or one hour of chemotherapy respectively. The molecular weight of palonosetron is (332.87) both hydrophilic and lipophilic in nature, with a half-life of 40 hours, approx. 62% protein binding. With all these good drug properties palonosetron is a drawback of poor bioavailability i.e., (50%)4. This study is aimed to develop medicated oral jelly of palonosetronto improve drug bioavailability.

MATERIALS AND METHODS:

Palonosetron hydrochloride was obtained from Incepta pharmaceutical, Ltd. Trisodium citrate and Glycerine were obtained fromSquare pharmaceutical Ltd. Citric acid and Methylparaben were obtained from ACME Laboratories Ltd.

Formulation of medicated jellies loaded with **Palonosetron hydrochloride**:

Heating and congealing methods were used to formulate jellies. 66.7 gm of sugar is taken in beaker a to form a sugar syrup, with the addition of 100 ml of water. All ingredients which are listed in table number 1 were weighed accurately and mixed properly. Which is heated at 80 °C temperature with continuous stirring.

After complete dissolution of gelling agent citric acid and stabilizer were added which is followed by stirring, which will improve the softness of the jellies, followed by boiling for few a minutes with maintaining pH. Preservatives were added to the solution with proper mixing. The next step was the addition of a drug i. e. palonosetron into the solution. The drug was weighed accurately and added to the above solution with proper mixing. In the last step drug-loaded solution was transferred into jellies moulds to cool down and transform in the forms of jellies. Moulds were covered properly to avoid any type of contamination5-9.

**Table 1: Different formulationsof Palonosetron hydrochloride loaded medicated jellies.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Ingredients (in %) | MJ1 | MJ2 | MJ3 | MJ4 |
| Xanthan gum | - | 0.5 | 1 | 0.8 |
| Trisodium citrate | 3.3 | 3.0 | 2 | 2.8 |
| Glycerin | 3 | 3 | 3 | 3 |
| Citric acid | 2 | - | 2 | - |
| Methyl paraben | 0.18 | 0.18 | 0.18 |  |
| Sucrose | 50 | 50 | 50 | 50 |
| Sodium benzoate | 0.01 | 0.01 | 0.01 | 0.01 |
| Strawberryﬂavour | 0.1 | 0.1 | 0.1 | 0.1 |
| Water | 20 | 20 | 20 | 20 |

Evaluations of drug-loaded jellies:

1-**Physical observation**

All drug-loaded jellies were analysed for different types of physical testing like the texture of jellies,(on the bases of stickiness and any type of grittiness by rubbing between fingers type of change in odor and visually analyzed for clarity11-13.

2-**Weight variation**

For the estimation of variation in weight, ten formulations were taken and weighed to find out average weight. A variation was monitored from average weight and individual weight14-16.

3- **Determination of pH**

With the means of digital pH meter, pH of the formulations was estimated. Jelly was dissolved in water and after it **pH** was observed17-18.

3-Spreadability:

To determine the spreadability of drug-loaded jellies multimer suggested apparatus was used after fabrication. It was estimated based on the slides separation having jelly formulation19,20.

4-Viscosity Study:

Viscosity of the prepared jelly formulations was measured by the means of Brookfield viscometer21,22.

5-Content Uniformity:

prepared jelly formulations were dissolved in 50 ml of phosphate buffer pH 6.8. Absorbance was measured by the means of UV visible spectrophotometer23.

6-**Syneresis:**

Syneresis or de-swelling is a characteristic of gels by releasing of liquid which cause shrinkage of gels resulting in quality reduction of formulation24.

7-In-vitro Dissolution Study:

USP paddle-type apparatus was used for this study. Phosphate buffer was used as dissolution medium (900ml), temperature was maintained at 37 °C and 100 rpm. Samples withdrawn periodically and absorbance was checked by means of UV visible spectrophotometer12,13.

**Table 2:outcomes of evaluation parameters of different drug loaded jelly Preparations.**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Batch code | Appearance | Consistency | %Drug content (n=3) | % Weight variation | pH  (n=3) | Viscosity  (cps) (n=3) | Spreadability | Syneresis |
| MJ1 | Smooth and very soft | Cloudy | 93.06±0.53 | 4.46±0.34 | 6.61±0.07 | 589937 | 24 | 6.48±0.08 |
| MJ 2 | Smooth and firm | Cloudy | 92.92±0.36 | 5.68±0.25 | 6.63±0.06 | 633422 | 28 | 6.35±0.02 |
| MJ 3 | Smooth | Transparent | 97.23±0.38 | 5.43%±0.08 | 6.72±0.07 | 707869 | 25 | 6.62±0.05 |
| MJ 4 | Very soft | Transparent | 90.52±0.66 | 5.33%±0.12 | 6.83±0.02 | 658924 | 30 | 6.83±0.07 |

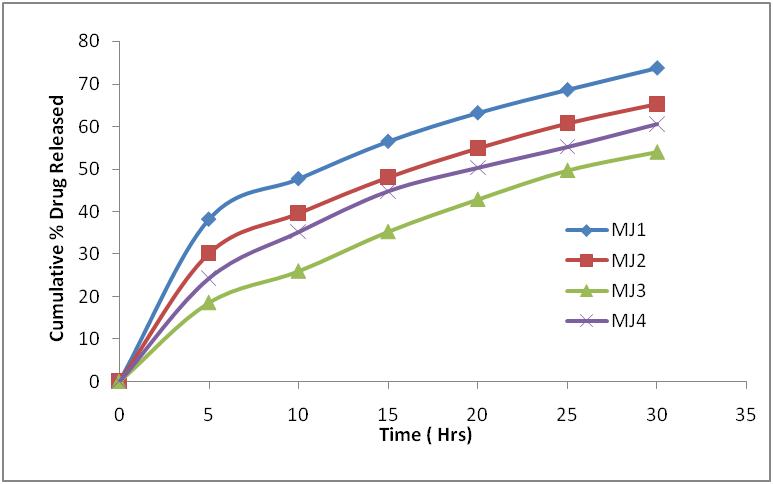


Figure 1: *In-vitro* release of medicated jellies.

T**able 3: Stability studies results of drug loaded jellies**

|  |  |  |  |
| --- | --- | --- | --- |
| Formulation | Month | pH | Viscosity |
| MJ1 | 1 | 6.41±0.04 | 589937 |
| 2 | 6.38±0.07 | 579834 |
| 3 | 6.22±0.02 | 569430 |
| MJ2 | 1 | 6.63±0.06 | 633422 |
| 2 | 6.49±0.04 | 622420 |
| 3 | 6.53±0.08 | 612220 |

**RESULTS AND DISCUSSION**

For justification purpose of patient acceptance of formation and patient compliance, the formulation should be physically observed in a proper way. Among all the formulations MJ1 was found best with regards of smoothness and softness, MJ1 was found a little sticky but is within an acceptable limit.MJ2 formulation showed fluid-like consistency.MJ3 and MJ4 preparation were thick in consistency. Weight variation was found between 4.46±0.34% and 5.68±0.25% in all prepared jelly formulations.

The pH of the drug-loadedpreparations was found in the range of 6.22±0.02 to 6.63±0.06which was slightly acidic. Sucrose may cause precipitationwith citric acid on standing14. Therefore, a minimum amount of citric acid was added just to maintain the pH.

Syneresis was checked after 24 h of the jelly formulation. No formulation showed syneresis at room  
temperature (25°C ± 5°C).The batch MJ1 has shown 79.22% and batch MJ2 has shown 71.65 % release within 30 min.

The jelly preparation of batch MJ1 and MJ2 were checked for a change in various parameters for example appearance, pH, and viscosity for 3 months. A freshly made jelly sample was taken as a reference standard for evaluating all parameters. The result of short-termstability studies mentioned in Table 3 depicts no significant changes in pH and appearance in theoptimized jelly formulations of batches MJ1 and MJ2 with time.Formulation MJ1depictsbest results.

CONCLUSION:

Above study was an attempt to formulate and evaluate palonosetron hydrochloride-loaded jellies.

Four formulations were formulated using the heating and congealing method. MJ1 was found best formulation among all formulations. The above study can be concluded in the successful delivery of palonosetron in the form of jelly.

**Conflict of interest:**

No conflict of interested is associated with this work.

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