# Formulation, Evaluation and release rate characteristics of medicated jelly of vitamin C

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**Abstract**: Medicated jelly formulations are patient friendly dosage form for pediatric, geriatric and dysphagic patients. These formulations offer rapid dissolution and absorption of drugs through oral mucosa therefore show the early onset of action. The objective of the study was to develop and evaluate oral jelly formulations of vitamin C. Slurry method was adopted using glucose 103gm, sugar 67gm, gelatin 10gm and sorbitol 6.56gm. Preformulation studies were performed including the organoleptic profile, pH, and solubility of both drugs. The medicated jelly of Vitamin C was prepared and evaluated for physical characteristics, weight variation, syneresis, pH, taste and palatability, drug content, release rate characteristics and stability studies. All the jellies were found to have patient welcoming taste and were palatable. All formulations showed more than 50% drug release within 15 minutes, while 93% drug was released in 30 minutes. The results of release kinetics showed that the formulation followed the zero order release kinetics. Thus the drug was released at constant rate independent of the drug concentration involved in the process. All the medicated jellies were found to remain stable stored for 60 days at different temperatures. The present study revealed that medicated jellies of vitamin C could be employed orally in an effective form as an alternative solid oral dosage form for special population such as pediatrics, geriatrics and patients with dysphagia.

**Keywords**: Medicated jelly, vitamin C, ascorbic acid, artificial saliva, drug release kinetics.

## INTRODUCTION

The progress of pharmaceutical product is based upon the choice of appropriate drug delivery system. Considerable attention has been focused on the development of novel drug delivery system as it provides additional benefits for patients. The clinicians and patients preferred the oral route due to various reasons amongst which foremost is the ease of its administration (Chien & Swarbrick, 1992).

The palatable and elegant medicated jelly is accepted as a drug delivery system because children don't show interest in taking medication, and need so much counseling to the mothers to use the formulations in the right directions to their babies (Bhusan *et al*., 2000). Due to the softness and smoothness in its texture the jellies can be masticated easily by children as well as by the patients of advanced age. Medicated jellies stimulate release of salivary fluids thus helps in conditions like xerostomia. Medicated jelly today is gaining consideration as a "vehicle" or a "delivery system" to administer active principles that can improve health and nutrition. US market accounts for approx. 20% of world market for medicated jelly. The jellies as dosage form can be preserved in cool place or at room temperatures as well as its appearance remain secured (Yokoyama *et al*., 2004).

In the current study, vitamin C was used in combination in the medicated jelly. The structure of Vitamin C is shown in the fig. 1. It is freely soluble in water and sparingly soluble in ethanol. It is practically insoluble in ether and chloroform (Remington, 1970).

The objective of this study was to formulate the oral medicated jelly of vitamin C by using suitable optimization technique and to optimize the drug release profile and as well as to evaluate the optimized formulations for various in vitro parameters like in vitro dissolution, odor, taste and palatability, pH, viscosity, syneresis, studies etc. The stability studies also performed on these optimized formulations as per ICH guidelines.

## MATERIALS AND METHODS

### *Chemicals*

All the chemicals used in this study, were of analytical grade. Vitamin C was gifted by ZAKFAS

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pharmaceuticals (Pvt.) Ltd., liquid glucose and sugar from Rafhan Faisalabad. Starch and sorbitol from Malaysia through Habib essence, gelatin from Lahore gelatin, orange flavor from Silicia Flavor Company, cooking oil from HOM Quality Foods Pvt Ltd and Hydroxyl naphthol blue disodium salt from SIGMA-ALDRICH AG industries trasse (Switzerland).

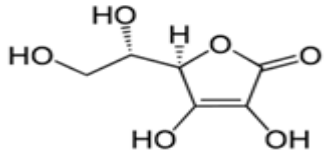


**Fig. 1**: Chemical structure of vitamin C

***Preparation of medicated jellies***

According to Volka Food International, medicated Jellies were prepared by using following ingredients (table 1).

***Standard curve for vitamin C***

100mg of vitamin C dissolved in 100 to prepare stock solution. Different dilutions were prepared in a concentration of 5µg, 10µg, 15µg, 20µg, 25µg, 30µg, 35µg, 40µg and 45µg of drug in solvent respectively and were then analyzed for the absorbance at the 265nm with UV spectrophotometer (Perkin Elmer lambda 25) (fig. 2).

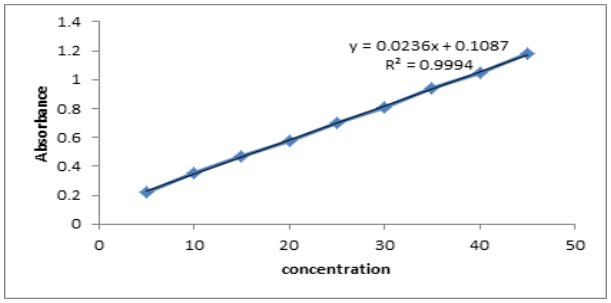


**Fig. 2**: Calibration curve for vitamin C

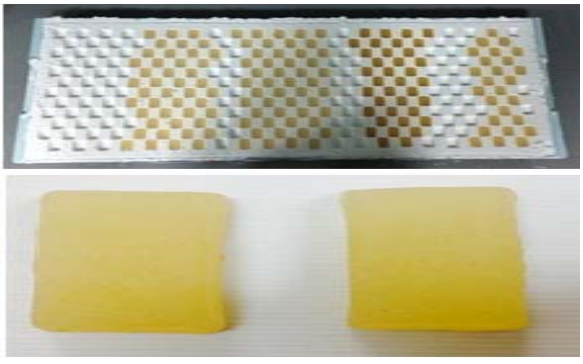

**Fig. 3**: (A) Setting of medicated jellies in starch moulds (B) Medicated jellies of Vitamin C

***Preparation of phosphate buffer saline***

A 1000ml cleaned and dried volumetric flask was taken to prepare the 1000ml phosphate buffer saline (Pharmacopoeia, 2002). All the ingredients were dissolved completely until clear solution was obtained and final volume was made by addling sufficient quantity of distilled water up to 1 liter mark and the pH was confirmed to be 7.4.

***Preparation of artificial saliva***

The artificial saliva was prepared by the method reported by Van Ruth and his coworkers (Van Ruth *et al*., 2001) (table 2)

***Solubility of vitamin C***

For determination of solubility of vitamin C, cleaned and dried six conical flasks having capacity of 50ml were taken and numbered as 1st, 2nd and 3rd. Then 5ml of menthol, phosphate buffer saline (at pH 7.4) and distilled water separately added in each flask. Then 1gm of vitamin C was added in the each flask. The mixture in each flask was stirred by thermostatically controlled stirrer at constant temperature 37Ċ for 48 hrs (table 3).

***Partition coefficient studies of vitamin C***

In a 100 mil separating funnel 5ml of distilled water and octanol were added. Pinch of vitamin C was added in the separating funnel and shaken vigorously for 10-15 minutes. Then separate water and octanol layers in test tubes. The absorbance of each layer was measured at 265nm by UV spectrophotometer. The volumetric flask of 1liter was taken and sufficient amount of water was added in it. Then all ingredients were added in it one by one and stirred continuously. Then final volume of 1litre was made by adding distilled water up to the mark and was filtered through Whattmann filter paper (Van Ruth *et al*., 2001).

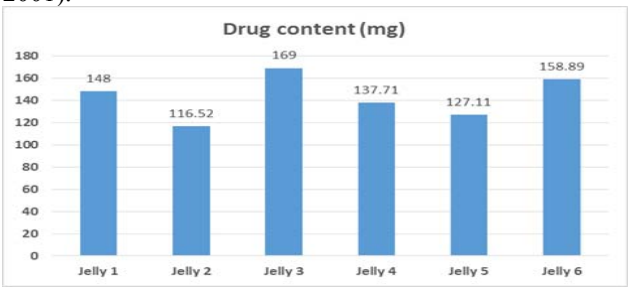


**Fig. 4**: Graphical representation of Vitamin C content present in jellies Release rate characteristics of vitamin C from jellies

***In vitro evaluation of prepared medicated Jellies***

*Physical observations*

The medicated jellies were evaluated visually for the clarity, color, odor, presence of any type of particles and texture. The texture was evaluated in terms of stickiness by mild rubbing the gel between two fingers. Appearance must be appealing for the patient compliance and acceptance (table 4).

***Syneresis***

All the jellies were observed for signs of syneresis at room temp (25°C±5°C) and 8°C±1°C. The formulations

showing signs of syneresis were rejected and not considered for further studies (Suda *et al*., 2005) (table 5).

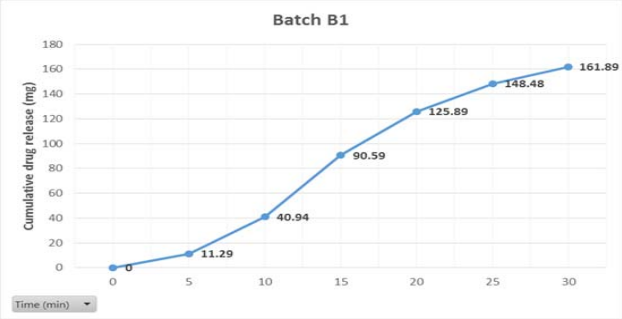


**Fig. 5**: Average cumulative drug release in given time intervals from vitamin C jellies

***Determination of pH***

The pH of prepared jellies was measured using a digital pH meter at room temperature (25°C±5°C). For this purpose, unit dose jelly was dispersed in 25 ml of distilled water to make a 1% solution, and the pH was noted (Covington *et al*., 1985).

**Table 1**: Ingredients Used in Medicated Jellies

| 1st portion | | 2nd portion | |
|---|---|---|---|
| Ingredient | Quantity | Ingredient | Quantity |
| Water | 9 gm | Gelatin | 10 gm |
| Liquid Glucose | 103 gm | Sorbitol | 6.56 gm |
| Sugar | 67 gm | Water | 64 gm |
| | | Vitamin C | 10 gm |

**Table 2**: Composition of artificial saliva

| Ingredients | Quantity |
|---|---|
| NaHCO3 | 5.208g |
| K2HPO4.3H2O | 1.369 g |
| NaCl | 0.877 g |
| KCl | 0.477 g |
| CaCl 2 .2H2O | 0.441 g |
| Water | qs 1 litre |

**Table 3**: Summary of solubility Vitamin C

| Solvents | Solubility of Vitamin C |
|---|---|
| Water | Freely soluble |
| PBS | Freely soluble |
| Methanol | Sparingly soluble |

***Taste and palatability***

It was carried out on a trained panel of six healthy adult human volunteers of age group 20-32 years and body weight 56-70kg. The study protocol followed the ethical principles for medical research involving human subjects. The bitterness was recorded immediately and at intervals of 1 min up to 10 min (Khan *et al*., 2007) (table 6).

***Weight variation***

Ten jellies were taken and the weight of individual jellies was determined by using weighing balance of analytical grade.

***Stability studies***

For the stability studies jelly, formulations were packed in aluminum foils, transferred to high-density polyethylene containers, tightly closed, and stored at room temperature (25°C±5°C), (8°C±1°C) and (40°C± 2°C) for 60 days (European Medicines Agency 2003). The samples were characterized for change in various parameters such as appearance, pH, sugar crystallization, stiffness, and syneresis at the end of 60 days. Readings of freshly made jellies were used as a reference standard for subjective evaluations (table 7).

***Determination of drug content and content uniformity of vitamin C***

Drug content of 6 medicated jellies was determined and compared (Salunke, 2013). The drug content was calculated by using calibration curve (fig. 4).

***Release rate characteristics of vitamin C***

For vitamin C the artificial saliva, was used as dissolution medium maintained at 37°C±0.5°C.The unit dose jelly was masticated by using artificial masticator in the respective dissolution medium. 5mL samples were withdrawn at 5, 10, 15, 20, 25 and 30 minutes. The sample was replaced by an equal volume of respective dissolution medium to maintain constant volume throughout and analyzed at 265nm. The mechanism of drug release from jellies was analyzed by fitting the data into zero-order, first-order, Highuchi and Koresmeyer-Peppas kinetic models (Ritger PL &Peppas NA, 1987).

Zero-order release equation $Q_t = K_0\, t$
First order equation $\text{Log}\, Q_t = \text{Log}\, Q_0 - K1\, t$
Higuchi equation $Q_t = KH\, t_{1/2}$
Hixson-Crowell equation $Q0_{1/3} - Qt_{1/3} = KHC\, t$
Korsmeyer-Peppas equation $Mt / Mo = Kspt^n$

## RESULTS

The solubility profile of vitamin C in different solvent was assessed as shown in table 3. The jellies were evaluated for the clarity, colour, odor, presence of any type of particulate matter stickiness are summarized in table 4. While the results of signs of syneresis at different temperatures i.e. (25°C±5°C) and 8°C±1°C and 40°C of the jellies are shown in the table 5. The pH of the prepared formulations was found in the range of 3.45 to 4.50 which was acidic as shown in table 7. Stability studies of the jelly formulations were performed and are shown in table 7. Likewise, the average and cumulative drug release pattern of vitamin C jellies are demonstrated in table 8.The final step of the study was the release kinetics of vitamin C jellies which are shown in table 9.

**Table 6**: Taste and palatability of jellies

| Time | Medicated jellies |
|---|---|
| After 1 minute | Sweet & palatable |
| After 2 minute | Sweet & palatable |
| After 3 minute | Sweet, slightly sour & palatable. |
| After 4 minute | Sweet, acceptable sour & palatable |
| After 5 minute | Sweet, acceptable sour & palatable |
| After 6 minute | Sweet, slight tartrate & palatable |
| After 7 minute | Sweet, slight tartrate & palatable |
| After 8 minute | Sweet, slight tartrate & palatable |
| After 9 minute | Sweet, slight tartrate & palatable |
| After 10 minute | Sweet, slight tartrate & palatable |

## DISCUSSION

Vitamin C is found to be freely soluble in distilled water and PBS while slightly soluble in methanol as in table 3. Result of solubility studies as shown in table 3 indicates that as the conc. of methanol in water increases the solubility of drug in the resulting mixture of solvents decreases but still sufficient quantity of drug is soluble in water that will help drug to dissolve in saliva.

Following formula was used for determination of partition coefficient:

$$Partition\ Coefficient\ for\ the\ drug\ (KP) = \frac{Conc\ of\ drug\ in\ Org\ Phase}{Conc\ of\ drug\ in\ aq\ phase}$$

Logarithmic value (Log P o/w) of Partition coefficient of vitamin C was found and equals to (-2.15). Partition coefficient of calcium gluconate was found to be (LogPo/w) -7.51. The result revealed that the given drugs have enough hydrophilicity which is considered significant for formulation to rapidly dissolve in saliva.

The jellies were evaluated for the clarity, colour, odor, presence of any type of particulate matter stickiness are summarized in table 4. All the jellies were transparent. The jellies were slightly liquid to thick in nature with varying degrees of consistency. A non-sticky texture was observed in the formulations. Their color and odor were in an acceptable range. The results of signs of syneresis at different temperatures i.e. (25°C±5°C) and 8°C±1°C and 40°C of the jellies are shown in the table 5 given below. All the formulations have shown signs of syneresis so the prepared medicated jellies were considered for further studies.

The pH of the formulation influences the taste and stability of oral jellies. The pH of the prepared formulations was found in the range of 3.45 to 4.50 which was acidic as shown in table 7. The minimum quantity of citric acid was added just to maintain the pH. The results of taste and palatability studies of formulations on human volunteers are presented in the table 6 given below. All the volunteers reported the jelly formulations as non bitter. The formulations showed better palatability. The reason of reduction of tartartness of vitamin C in jellies could be due to lower diffusion of vitamin C by gelling agents from the jelly to the taste buds. Sweetness and flavor were variable but in acceptable limits .Orange flavor was chosen to make the jellies palatable (Gohel MC, Parikh RK, 2009).

The results of taste and palatability of 10 jellies are shown in the table 6. The results showed that weight of the jellies varied from 3.35 to 4.08 whereas average weight of jellies was 3.707.The results of stability studies on jelly formulations are given in the following table 7. The results of stability studies showed that all the formulations remain stable with respect to the parameters like appearance, pH, sugar crystallization, stiffness, and syneresis at the end of 60 days at various temperatures ranges.

The results of release of drug from jellies of prepared batch are given in the following table 8.

The results of drug release kinetics are given in table 9 which showed that medicated jelly follow the zero order release kinetics. Thus the drug is released at constant rate independent of the drug concentration involved in the process**.**

The results of release kinetics show that the prepared formulations vitamin C follows zero order release kinetics. Thus the drug is released at constant rate independent of the drug concentration involved in the process.

**Table 4**: The results of physical appearance of jellies

| Formulation | Clarity | Color | Odor | Particulate matter | Stickiness |
|---|---|---|---|---|---|
| vitamin C medicated jelly | Acceptable | Dark rattan beize | Pleasant | No | No sticky |

**Table 5**: Results of syneresis of jellies

| | Syneresis | | |
|---|---|---|---|
| Formation of Vit.C+Calcium gluconate Jelly | 8°C | 25°C | 40°C |
| | NO | NO | NO |
| | Mild Contraction, no water separation | No Contraction, No Water Separation, proper texture | No Contraction, No Water Separation, proper texture |

**Table 7**: Stability studies of jellies of at various temperatures

| Parameters | Temperature (25°C ± 5°C) | Temperature (8°C ± 1°C) | Temperature (40°C ± 2°C) |
|---|---|---|---|
| Appearance | clear, smooth & soft texture. | Clear, smooth & soft texture. | Clear, smooth & soft texture. |
| pH | 3-3.2 | 3-3.2 | 3-3.3 |
| Sugar crystallization | No | No | No |
| Stiffness | Acceptable | Acceptable | Acceptable |
| Syneresis | No | No | No |

**Table 8**: Average and cumulative drug release in given time intervals from vitamin C jellies

| Time interval | Jelly 1 | Jelly 2 | Jelly 3 | Average drug release | Cumulative drug release |
|---|---|---|---|---|---|
| 0-5 min | 10.59 | 14.83 | 8.47 | 11.29 | 11.29 |
| 6-10 min | 27.54 | 31.77 | 29.66 | 29.65 | 40.94 |
| 11-15 min | 48.75 | 44.49 | 55.05 | 49.44 | 90.59 |
| 16-20 min | 36.01 | 36.01 | 33.89 | 35.30 | 125.89 |
| 21-25 min | 21.18 | 25.42 | 21.18 | 22.59 | 148.48 |
| 26-30 min | 14.83 | 10.59 | 14.83 | 13.41 | 161.89 |

**Table 9**: Release kinetics of vitamin C jellies

| Zero order Kinetics | | First order Kinetics | | Higuchi kinetics | | Hixon-crowell kinetics | | Korsmeyer Pappas kinetics | |
|---|---|---|---|---|---|---|---|---|---|
| $R^2$ | $K_0$ | $R^2$ | $K_1$ | $R^2$ | $K_h$ | $R^2$ | $K_{hc}$ | $R^2$ | N |
| 0.9864 | 5.675 | 0.8786 | 0.124 | 0.9312 | 25.692 | 0.9174 | 0.030 | 0.9859 | 1.089 |
| 0.9834 | 5.524 | 0.8917 | 0.123 | 0.9368 | 25.118 | 0.9278 | 0.030 | 0.9831 | 1.023 |

## CONCLUSION

In the present study, the jellies loaded with vitamin C were successfully formulated using gelatin as gelling agent. The formulations showed acceptable physico-chemical properties and stability. Thus it was revealed that the medicated jellies of vitamin C could be employed orally in an effective form for pediatric, geriatric and dysphagia patients as alternatives to other solid oral dosage forms.

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