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# Development of Taste Masked Oralgel of Sertraline-Hydrochloride

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## Abstract:

Sertraline hydrochloride is very bitter in taste. Use of gel forming agent, which lowers the diffusing out of drug in the oral cavity was used as development strategy. Taste masked Sertraline HCl (SRT) oral gel formulation was developed using Gellan gum as gelling agent. Gellan Gum alone could not give the desired properties with such a high amount of co solvents, hencePectin was used in adjuvant to gellan gum. Mannitol was used as diluent for thegel formulation. Glycerol & PEG-400 were used as solubilizing agent for the Sertraline hydrochloride. Methyl paraben & Propyl paraben were used as preservative. Citric acid & Sodium citrate buffers were used to maintain the pH 7 to 7.5. Acesulfame potassium was used as sweetener. Orange flavor was used to enhancethe overall mouth feel.

*Keywords* — **Sertraline hydrochloride,Gel .**

## INTRODUCTION

Sertraline HCl is a selective serotonin reuptake inhibitor (SSRI) antidepressant and anxiolytic agent. The oral bioavailability of Sertraline is about 45% because of extensive first pass metabolism in liver and gut wall. Buccal routes of drug delivery offer distinct advantages over oral administration for systemic drug delivery. These advantages include possible bypass of first pass effect, avoidance of pre-systemic elimination within the GI tract, these factors make the oral mucosal cavity a very attractive and feasible site for systemic drug delivery . Moreover buccal drug absorption can be promptly terminated in case of toxicity by removing the dosage from the buccal cavity therefore mucoadhesive drug delivery devices such as patches,tablets, films, gels ointments and discs were suggested. Thus sertraline HCl was selected as a model drug for investigation because of its suitable properties like dose strength , halflife (6hrs) and molecular weight (342.69 g/mol)[1]. In the present development work taste masked oral gel formulation was formulated.

## EXPERIMENTAL METHODOLOGY

### a) Formulation of oral gel:

Solubility studies were performed with different solvents & it was observed that 20 % of PEG 400, 20 % of Glycerol and 60 % of water gives the maximum solubility of sertraline Hydrochloride. Hence this system was considered ideal for the formulation of gel dosage form. All the required ingredients of the formulation were weighed accurately. Dry gellan gum powder and pectin powder was dispersed in 30 ml of distilled water

maintained at 95°C. The dispersion was stirred at $95^0$C for 30 min using a magnetic stirrer to facilitate hydration of gellan gum. PEG 400 and Glycerol was added under stirring. The required amount of Mannitol was added to the solution with continuous stirring and the temperature was maintained above 80°C. Sertraline hydrochloride was added with stirring. Then citric acid and preservatives (methylparaben, propylparaben) were added with stirring. Finally, required amount of sodium citrate was dissolved in 10 ml of distilled water and added to the mixture. At last orange flavours and Colour sunset yellow was added. The weight of the gel was monitored continuously during manufacturing and finally it was adjusted to the 100 gm with distilled water. 5 grams of the mixture containing gellan gum, pectin, sertraline hydrochloride and other additives was added to aluminum cups. The mixture was allowed to cool to room temperature to form gel. The final formulation composition of the formulation is given below in Table 1:

Table 1: Final composition of the Gel dosage form

| **Ingredients** | **Final Formulation** |
|---|---|
| Sertaline Hydrochloride | 2.8% |
| PEG 400 | 20 % |
| Glycerol | 20% |
| Mannitol | 10 % |
| Gellan Gum | 0.5 % |
| Pectin | 0.1 % |
| Orange flavours | 2 % |
| Aspartame | 1 % |
| Colour Sunset yellow | 0.25 % |
| Citric acid | 0.5 % |
| Sodium citrate | 0.3 % |
| Methyl Paraben | 0.1 % |
| Propyl Paraben | 0.01 % |
| Water | q.s. |

**b) Evaluation of oral gel :**

Texture of the soft gel was evaluated in terms of stickiness and grittiness by mildly rubbing the gel between two fingers. Viscosity of the soft gels was measured using Brookfield DV-II+Proviscometer (spindle number LV4 at the rotation of 50 rpm at room temperature).The pH of sertraline hydrochloride soft gel was measured using Electroquip digital pH meter at the room temperature. Syneresis is one of the major problems associated with low acylatedgellan gum gels. Gels were kept under scrutiny for signs of syneresis. Drug Content of the gel was determined by UV spectrophotometer. *In-vitro* drug release of the prepared gel was performed in simulated

gastric fluid (SGF), USP dissolution apparatus 2 using paddle at a speed of 100 rpm using SGF as dissolution media at 37±2°C. For the evaluation of taste masking the gel was subjected to dissolution studies in pH 6.8 (SSF) at 37 $^{0}$ C for 1 hour and 50 rpm . The initial time points of 1 minute and 5 minute were considered to be important to determine the efficiency of taste masking. Human volunteers were requested to taste the five gram of gel by keeping in the mouth for 30 sec and rank it on a scale of perception ranging from 0-5.

**c) Stability Assessment of Gel**

A physically stable oral gel retains its viscosity, color, clarity, taste, and odor throughout its shelf-life. Gels were checked for syneresis during storage. A freshly made sample should serve as a reference standard for subjective evaluations. The samples were kept at different temperatures (0-8°C and room temperature) for 2 months. The samples of soft gel were observed for pH, viscosity, and appearance at the interval of one week. All the measurements were performed after allowing the samples to be equilibrated at 25°C for two hours.

## RESULT AND DISCUSSION

### a) Evaluation of physicochemical parameters of gel :

Various physicochemical parameters of final formulation are summarized in table 2.

Table 2: Physicochemical parameters of taste masked Sertraline Hydrochloride Gel

| **Parameters** | **Observed values** |
|---|---|
| | |
| Texture evaluation (Appearance) | Smooth transparent gel. Non sticky and non-gritty in nature. |
| Viscosity | 8125-9112 CPS |
| pH | 7.02 |
| Syneresis | Does not show syneresis on keeping. |
| Drug content | 100.9 % |
| In-vitro release study (min) 900 ml SGF at 100 RPM, Paddle | % Dissolution |
| 15 min | 65 % |
| 30 min | 88 % |
| 45 min | 100 % |

### b) Evaluation of taste masking

The taste evaluation by Spectrophotometric method indicated that no drug release is observed at 1 min and 5 min in simulated salivary fluid at 37 0 c which indicates that the threshold bitter concentration of Sertraline hydrochloride wont be perceived in the saliva of the patient. The results of taste evaluation are shown in Table 3. All the thirty volunteers perceived the soft gel as non-bitter. The probable reason is that the gelling agents can lower diffusion of bitter substances from the gel to the taste buds. Mannitol and aspartame was selected as a sweetener in soft gel to mask the taste of Sertraline giving it a pleasant effect. Orange flavor was selected because to certain extent it helps in masking the bitter taste of drug and also improves patient acceptance.

Table 3: Evaluation of taste masking of gel by panel

| Preparation | No of volunteer rating the preparation as | | | | | |
|---|---|---|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 | 5 |
| Gel dosage form | 21 | 9 | | | | |

0 =Good, 1 = Tasteless, 2 = slightly bitter, 3 = Bitter, 4 = very Bitter, 5 = Awful

### c) Stability Assessment of Gel

Table 4 describes the stability data of the gel formulation.

Table 4: Stability of gel Dosage form

| Gel | Initial | 1M | 2M |
|---|---|---|---|
| Appearance | Clear | Clear | Clear |
| Assay | 99.7 | 98.5 | 98.7 |
| pH | 7.02 | 7.11 | 7.13 |
| Viscosity | 8325 | 8412 | 8990 |
| Taste | O.K. | O.K. | O.K. |

The results of short-term stability studies, shown in Table 4, indicated insignificant changes in pH, viscosity, and appearance in the optimized formulation with time. Also, syneresis was not observed in any of the samples at both temperatures. Therefore, it is recommended that soft gel should be stored at about 25°C.

## CONCLUSION

Taste masking by incorporation of Sertraline hydrochloride in swellable matrix such as combination of gellan gum and pectin was found to be satisfactory. The gel holds the drug for sufficient time in the gel matrix while the dosage form is in the oral cavity and hence the bitter taste of Sertraline hydrochloride is not perceived. The

palatability of the gel was further improved by using suitable flavourants and sweeteners.

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