A Study on the Potential of Kappa-carrageenan and Carboxymethylcellulose in Extended Release Potassium Chloride Capsules

Apolinario, M.¹, Canlas, K.¹, Galang, J.¹, Gatus, G.¹, Genson, B.¹, Bayquen, A.¹, Carigma, A.¹

¹Faculty of Pharmacy, University of Santo Tomas, España, Manila
Potassium Chloride

• The drug of choice in preventing or treating hypokalemia (potassium deficiency)

• Major cation of intracellular fluid and is essential for the conduction of nerve impulses in heart, brain, and skeletal muscle

• Sudden release of potassium chloride in the stomach causes local irritation. (Kumar et al., 2011)
Kappa-carrageenan

• A natural marine colloidal gum that is extracted from seaweeds (Euchema spp) belonging to the Class Rhodophyceae or red algae

• Philippines is one of the main producers of carrageenan. (Food and Agriculture Organization of the United Nations, 2014)

• Used to gel, thicken or suspend, therefore it is also used in emulsion stabilization, for syneresis control, for bodying, binding and dispersion
Carboxymethylcellulose

• White, fibrous, free-flowing powder anionic polymer

• Readily soluble or dispersible in water of alkaline solutions to form highly viscous solutions useful for their thickening, suspending and stabilizing properties

• Widely used in many industrial aspects and also in laboratory due to its good biocompatibility
Extended Release

• “Extended-release dosage form is a modified-release dosage form showing a slower release of the active substance(s) than that of a conventional-release dosage form administered by the same route.” (European Pharmacopoeia 8)
Statement of the Problem

• General
  – The study is concerned with the determination of the potential of predetermined 2:1 ratio of kappa-carrageenan and carboxymethyl cellulose as agents to the extended release potassium chloride (KCl) capsules.
Statement of the Problem

• Specific

1. Does the extended release potassium chloride (KCl) capsule with the 2:1 ratio of kappa-carrageenan and carboxymethyl cellulose conform to USP dissolution requirements for Extended-Release Dosage Forms?

2. Are the Potassium chloride, kappa- Carregeenan and Carboxymethyl cellulose compatible with each other according to the Differential Scanning Calorimetry method?
Significance of the Study

• To provide an extended-release potassium chloride capsule formulation with the use of the kappa-carrageenan: carboxymethyl cellulosic ratio (2:1)

• The extended-release potassium chloride drug product will lessen gastrointestinal tract irritation providing a better therapeutic outcome.
Objectives of the Study

• Formulation of an extended-release potassium chloride capsule by incorporating kappa-carrageenan and carboxymethylcellulose

• Determination of the compliance of kappa carrageenan: carboxymethyl cellulose potassium chloride extended release capsules with the specifications for extended release formulation

• Determination of the compatibility of the three main ingredients.
Conceptual Framework

**INPUT**
- Potassium Chloride
- Kappa-carrageenan
- Carboxymethylcellulose

**PROCESS**
- Microencapsulation of Extended-release Potassium Chloride using the best ratio of Kappa-carrageenan and Carboxymethylcellulose
- Dissolution Test
  - TGA
  - DSC
  - AAS

**OUTPUT**
- Extended-Release Microencapsulated Potassium Chloride
Scope and Limitations of the Study

• Potassium chloride was used as an active ingredient

• Focused on the development and testing of an extended-release potassium chloride capsule using the predetermined ratio (2:1) of kappa-carrageenan and carboxymethylcellulose.
Scope and Limitations of the Study

- Methods should dwell on determining whether the new formulation complies with pharmacopoeia standards on extended release capsules.

- In vivo test was not performed.
RESEARCH METHODS
Materials

- Biopolymers
  - Carboxymethylcellulose and kappa-carrageenan
- Anhydrous Ethanol (solvent)
- Deionized water (solvent)
- Potassium Chloride (active ingredient)
- Size 0 Capsules
Instruments

Sotax Dissolution apparatus
Memmert oven
Atomic Absorption Spectrophotometer (AAS)
PerkinElmer DSC 4000
PerkinElmer TGA 4000
Microencapsulation
Dissolution Testing

• Basket Method (Apparatus 1)

• Parameters for Extended release Potassium Chloride Capsules (USP 35)
  • 100 rpm
  • 37±0.5° C
  • 900 ml distilled water as dissolution medium
  • Not more than 35% of the labeled amount of KCl is dissolved in 2 hours
Dissolution Testing

• Aliquots of 5ml each were withdrawn from six samples at predetermined time intervals (15, 30, 60, 90, 120 minutes).

• Potassium concentration in the dissolution samples was measured through atomic absorption spectrophotometry performed in Qualibet Testing Services Corporation.
Thermogravimetric Analysis & Differential Scanning Calorimetry

• The formulation was subjected to Thermogravimetric Analysis using a PerkinElmer TGA 4000 prior to Differential Scanning Calorimetry with PerkinElmer DSC 4000 performed by the Research Center for the Natural Sciences (RCNAS) at the University of Santo Tomas.
Results - TGA

Figure 1. TGA showing the minimum temperature for the decomposition of mixture is 264.58°C with a percent weight loss of 5.65%
Results – DSC

- DSC results showed that the individual Heat Flow peaks of the formulation ingredients (Kappa-carrageenan, Carboxymethylcellulose and Potassium chloride) are comparable to the Heat flow peak of the formulation containing the mixture of the three constituents.
Figure 2. Graph on the mean concentration of the extended release potassium chloride capsule per time after dissolution test
Table 1. Comparison of the USP Specification to the Actual Process and Results

<table>
<thead>
<tr>
<th>PARAMETER</th>
<th>USP 35</th>
<th>ACTUAL</th>
</tr>
</thead>
<tbody>
<tr>
<td>DISSOLUTION MEDIUM</td>
<td>900 mL distilled water</td>
<td>900 mL distilled water</td>
</tr>
<tr>
<td>DISSOLUTION APPARATUS</td>
<td>Apparatus 1</td>
<td>Apparatus 1</td>
</tr>
<tr>
<td>RPM</td>
<td>100rpm</td>
<td>100rpm</td>
</tr>
<tr>
<td>TIME</td>
<td>2 hours</td>
<td>2 hours</td>
</tr>
<tr>
<td>TOLERANCES</td>
<td>Not more than 35% of the labeled amount of KCl is dissolved in 2 hours</td>
<td>66.32% of the labeled amount of KCl is dissolved in 2 hours</td>
</tr>
</tbody>
</table>
Results – Statistical Analysis

• To test if the concentrations differ between time intervals, One-Way ANOVA F test was used. There was no significant difference found among the concentrations per time interval. This means that the concentrations among different time intervals were statistically equal and there is a steady release of drug by the formulation over time.
Conclusion

• The three main ingredients, Potassium chloride, kappa-carrageenan, carboxymethylcellulose, exhibited compatibility.

• The predetermined 2:1 kappa-carrageenan and CMC ratio showed potential as extended release agents.
• The kappa-carrageenan: carboxymethylcellulose ratio to be used for extended-release KCl formulation should be further evaluated to meet the USP requirements.


The United States Pharmacopeia 35th Ed. Vol.1