Prevention of Cap-Locking of Syrup Product by Treating the Manufacturing Process with Citric Acid Monohydrate

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Abstract

The aim of the study was to prevent crystallization of sucrose on the bottle neck and cap of sugar syrup containing product by treating the manufacturing process of sugar syrup with citric acid monohydrate. Diphenhydramine Hydrochloride syrup was selected as model product for experiment. Sugar syrup (sucrose 66% w/w) and partially inverted sugar syrup in which sucrose 66% w/w was treated with citric acid monohydrate for partially conversion of sucrose into invert sugars were prepared and content of invert sugars for the both syrups were determined. Sugar syrup and citric acid monohydrate treated sugar syrup (partially inverted) were used to manufacture the selected Diphenhydramine Hydrochloride syrup product. The Diphenhydramine Hydrochloride syrup product, in which sugar syrup was used, was considered as control and in which, citric acid monohydrate treated sugar syrup (partially inverted) was used, was considered as test sample. Then experiments were designed in such a way that the prepared sugar syrup (control sample) and partially inverted sugar syrup (test sample) were spread on opened Petri dishes and also spread on the neck of filled bottle and inside caps and the bottles of control and test sample are again capped and were kept at room temperature for 2 week observation. Diphenhydramine Hydrochloride syrup product (both control & test sample) were spread on opened Petri dishes and also spread on the neck of filled bottle & inside caps and the bottles of control and test samples were again capped and were kept at room temperature for 2 week observation. At zero time and after two weeks, crystal growths of sucrose for each experiment were checked visually. No crystal was observed in opened Petri dishes and bottle necks of partially inverted sugar syrup and of Diphenhydramine Hydrochloride syrup product manufactured by using partially inverted sugar syrup where content of invert sugars is more than 75% w/w, but remarkable crystal growths were found in opened Petri dishes and bottle necks of sugar syrup and of Diphenhydramine Hydrochloride syrup product manufactured by using sugar syrup where content of invert sugars is less than 15% w/w.

Keywords: Cap-Locking of Syrup Product by Treating, Manufacturing Process, Citric Acid Monohydrate

1. Introduction

Sucrose is a natural sweetening agent, very soluble in water & crystallizes from the medium in the anhydrous form[1]. It consists of two monosaccharides, α-glucose and fructose, joined by a glycosidic bond (-o-). Hydrolysis of sucrose yields D-glucose and D-fructose; the process is called inversion and the sugar mixture produced is known as invert sugar because, although sucrose itself rotates plane-polarized light to the right, the mixture “inverts” this light by rotating it to the left. This inversion is achieved by heating a sucrose solution, and applying either a solution of acid or enzymes. The syrup is neutralized when the desired level of inversion is reached. Optical rotation for sucrose is [α]D=+66.4°, for glucose [α]D=+53°, for fructose [α]D=-92° and for resultant equilibrium mixture [α]D=-20.6°[2] (See Figure 1). Invert sugar has a lower water activity than that of sucrose, so inverts provide more powerful preserving qualities (shelf life). Sucrose is less soluble than glucose and fructose. Invert sugar is more hygroscopic, so it can be used to make a product that stays moist longer than if sucrose was used and is less prone to crystallization[3].

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1.1 Inversion reaction

![Diagram of sucrose to D-glucose and D-fructose conversion]

Figure 1: Chemical conversion of sucrose to D-glucose and D-fructose.

Invert sugar may be used as a stabilizing agent to help prevent crystallization of sucrose syrups[4]. Commercial liquid invert sugars are prepared as different mixtures of sucrose and invert sugar. For example total invert sugar is half glucose and half fructose, while 50% invert sugar (half of the sucrose has been inverted) is one-half sucrose, one-quarter glucose and one-quarter fructose. Invert sugar is used mainly by food manufacturers to retard the crystallization of sugar and to retain moisture in the packaged food.

1.2 Crystallization

Crystallization is the (natural or artificial) process of formation of solid crystals precipitating from a solution, melt or more rarely deposited directly from a gas[5]. Crystallization is also a chemical solid-liquid separation technique, in which mass transfer of a solute from the liquid solution to a pure solid crystalline phase occurs. The crystallization process consists of two major events, nucleation and crystal growth[6].

1.3 Nucleation

Is the step where the solute molecules dispersed in the solvent start to gather into clusters, on the nanometer scale (elevating solute concentration in a small region), that becomes stable under the current operating conditions[7]. These stable clusters constitute the nuclei. However when the clusters are not stable, they redissolve. Therefore, the clusters need to reach a critical size in order to become stable nuclei. Such critical size is dictated by the operating conditions (temperature, super saturation, etc.)[8]. It is at the stage of nucleation that the atoms arrange in a defined and periodic manner that defines the crystal structure. — note that "crystal structure" is a special term that refers to the relative arrangement of the atoms, not the macroscopic properties of the crystal (size and shape), although those are a result of the internal crystal structure[9].

1.4 Crystal Growth:

The crystal growth is the subsequent growth of the nuclei that succeed in achieving the critical cluster size. Nucleation and growth continue to occur simultaneously while the supersaturation exists. Supersaturation is the driving force of the crystallization, hence the rate of nucleation and growth is driven by the existing supersaturation in the solution. Depending upon the conditions, either nucleation or growth may be predominant over the other, and as a result, crystals with different sizes and shapes are obtained (control of crystal size and shape constitutes one of the main challenges in industrial manufacturing, such as for pharmaceuticals)[10]. Once the supersaturation is exhausted, the solid-liquid system reaches equilibrium and the crystallization is complete, unless the operating conditions are modified from equilibrium so as to supersaturate the solution again. Many compounds have the ability to crystallize with different crystal structures, a phenomenon called polymorphism. Each polymorph is in fact a different thermodynamic solid state and crystal polymorphs of the same compound exhibit different physical properties, such as dissolution rate, shape (angles between facets and facet growth rates), melting point, etc. For this reason, polymorphism is of major importance in industrial manufacture of crystalline products[11].

2. Materials & Methodology

2.1 Materials

Materials for sugar syrup: Sucrose (source: Al Khaleej, Dubai), Purified water (Gulf Pharmaceuticals, RAK).

Materials for partially inverted sugar syrup: Sucrose (source: Al Khaleej, Dubai), Citric acid monohydrate (source: Yixing-Union, China), Purified water (Dubai Pharmacy College).

Materials for Diphenhydramine Hydrochloride syrup: Diphenhydramine Hydrochloride (source: M/S Medex, UK), Ammonium chloride (source: M/S Merck, Germany), Menthol (source: M/S V.ManeFils S.A., France), Sucrose (source: Al Khaleej, Dubai), Sodium citrate (source: M/S ADM Ringaskiddy Co. Cork, Ireland), Citric acid monohydrate (source: Yixing-Union, China), Glycerol (source: M/S Symbiotica Spec Ingredients SDN, Malaysia), Sodium saccharin (source: M/S Anstead International, UK), Sodium benzoate (source: Al Khaleej, Dubai), H₂O Citric Acid (H⁺)
Raspberry flavor (source: Al Khaleej, Dubai), Ethanol 95% (source: Al Khaleej, Dubai), Caramel color 3M(source: M/S Cerestar Ltd, UK), Purified water (Dubai Pharmacy College). All materials conform to specifications of pharmacopoeia (BP, USP) and In-house requirement.

Machineries & apparatus: Weighing balance (Company: Mettler Toledo, Model No.: SB12001, Made in Switzerland), glass beaker (Pyrex, Germany), Product manufacturing vessel (capacity: 3 litre, pyrex, germany), Syrup manufacturing vessel (capacity: 3 litre, pyrex, germany), water bath (Memmert, UK), Ekato stirrer, measuring cylinder, pH Meter (company: Orion, uk), Glass petridish 60 mm, glass bottle with aluminum cap.

2.2 Methodology

Preparation of sugar syrup (66% w/w):

2 kg sugar syrup was prepared. First 0.68 kg of purified water was heated to 70°C±1°C in syrup manufacturing vessel in water-bath. Then 1.32kg of sucrose was dissolved in the hot water in manufacturing vessel with stirring. After that, the temperature was raised to 90°C±1°C. At this temp, the sucrose solution was heated for 45 minutes. Then the syrup was cooled to 40°C. Finally weight of sugar syrup was adjusted to 2kg with purified water and stir for 2 minutes. Thus sugar syrup was prepared and considered as control sample and labeled as batch no “A 001”.

Preparation of partially inverted sugar syrup (66% w/w):

2 kg partially inverted sugar syrup was prepared. First 0.66 kg of purified water was heated to 70°C±1°C in syrup manufacturing vessel in water-bath. 0.44 g of citric acid monohydrate was dissolved in 20g of purified water and added to the manufacturing container. Then 1.32kg of sucrose was dissolved in the hot water with stirring. After that, the temperature was raised to 90°C±1°C. At this temp, the sucrose solution was heated for 45 minutes. Then the syrup (inverted) was cooled to 40°C. Finally weight of sugar syrup (inverted) was adjusted to 2kg with purified water. Thus partially inverted sugar syrup was prepared and considered as test sample and labeled as batch no “A 002”.

Preparation of Diphenhydramine Hydrochloride syrup using sugar syrup:

2 Liter Diphenhydramine Hydrochloride syrup was prepared using sugar syrup (batch no. A 001). First 1.669 kg of sugar syrup from the batch ‘A001’ was added to the manufacturing vessel. 4.80 g of sodium benzoate, 3.920 g of saccharin sodium, 22.8 g of sodium citrate were dissolved in 75 g of purified water in a glass beaker and the solution was added to the manufacturing vessel with stirring. 4.4 g of citric acid monohydrate and 5.4 g of Diphenhydramine Hydrochloride were dissolved in 15 g of purified water in a glass beaker with stirring and the solution was added to the manufacturing vessel with stirring. 52.6 g of ammonium chloride was dissolved in 80 g of purified water in a beaker and added to the manufacturing vessel with stirring. 140 g of glycerol was added to the manufacturing vessel with stirring. 0.44 g of menthol and 2 g of raspberry flavor were dissolved in 10g of alcohol in a glass beaker and the flavor solution was added to the manufacturing vessel with stirring. Make up volume to 2 liter with purified water and stir for 15 minutes. Thus prepared syrup was considered as control sample and labeled as batch no “P 001”.

Preparation of Diphenhydramine Hydrochloride syrup using partially inverted sugar syrup:

2 litre Diphenhydramine Hydrochloride syrup was prepared using partially inverted sugar syrup (Batch no A 002). First 1.669 kg of partially inverted sugar syrup from the batch ‘A002’ was added to the manufacturing vessel. 4.80 g of sodium benzoate, 3.920 g of saccharin sodium, 22.8 g of sodium citrate were dissolved in 75 g of purified water in a glass beaker and the solution was added to the manufacturing vessel with stirring. 4.4 g citric acid monohydrate and 5.4 g of Diphenhydramine Hydrochloride were dissolved in 15 g of purified water in a glass beaker with stirring and the solution was added to the manufacturing vessel with stirring. 52.6 g of ammonium chloride was dissolved in 80 g of purified water in a beaker and added to the manufacturing vessel with stirring. 140 g of glycerol was added to the manufacturing vessel with stirring. 0.44 g of menthol and 2 g of raspberry flavor were dissolved in 10g of alcohol in a glass beaker and the flavor solution was added to the manufacturing vessel with stirring. Make up volume to 2 liter with purified water and the color solution was added to the manufacturing vessel with stirring. 6 g of caramel color was dissolved in 20g of purified water and the color solution was added to the manufacturing vessel with stirring. Make up volume to 2 liter with purified water and stir for 15 minutes. Thus prepared syrup was considered as control sample and labeled as batch no “P 002”.
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Physical test of syrups and syrup product:

Appearance and pH of sugar syrup, partially inverted sugar syrup, Diphenhydramine Hydrochloride using sugar syrup and Diphenhydramine Hydrochloride using partially inverted sugar syrup were checked and recorded. Determination of content of invert sugars in syrups:

Content of invert sugars for sugar syrup (batch no A001) & partially inverted sugar syrup (batch no A002) were determined by using the testing method of Invert sugar” BP 2007.

3. Design of Experiments
3.1 Experiment - A

Sugar syrup & partially inverted sugar syrup in opened Petri dish: 40g from each sugar syrup (batch no A001) & partially inverted sugar syrup (batch no A002) were kept in opened glass Petri dish at room temperature. Initial and 1 week observation for crystal growth of sucrose in the syrups at room temperature were monitored & results were recorded. Here sugar syrup & partially inverted sugar syrup were considered as control & test sample respectively.

3.2 Experiment - B

Diphenhydramine Hydrochloride syrup, which was prepared using sugar syrup, was considered as control and which, was prepared using partially inverted sugar syrup, was considered as test sample.

Diphenhydramine Hydrochloride syrup in opened Petri dish: 40 gm from each control (batch no P 001) and test sample (batch no P 002) were kept in opened Petri dish at room temperature. Initial and 1 week observation for crystal growth of sucrose were monitored & results were recorded.

3.3 Experiment - C

Sugar syrup and partially inverted sugar syrup spread inside cap and bottle neck: Sugar syrup (batch no A001) and partially inverted sugar syrup (batch no A002) were spread in glass bottles. Each bottle was capped. Cap of bottle of sugar syrup was spread then 1 g of sugar syrup was spread inside cap and bottle neck and the cap was again closed. Similarly, cap of bottle of partially sugar syrup was spread and then 1 g was spread inside cap and bottle neck and the cap was again closed. Initial and 2 week observation for crystal growth of sucrose in the syrups at room temperature were monitored & results were recorded.

3.4 Experiment - D

Diphenhydramine Hydrochloride syrup prepared using sugar syrup and partially inverted sugar syrup spread inside cap and bottle neck: Diphenhydramine Hydrochloride prepared using sugar syrup (batch no P001) & partially inverted sugar syrup (batch no P002) were filled in glass bottles. Each bottle was capped. Cap of Diphenhydramine Hydrochloride prepared using sugar syrup was opened and then 1 g of sugar syrup was spread inside cap and bottle neck and the cap was again closed. Similarly, cap of bottle of Diphenhydramine Hydrochloride prepared using partially inverted sugar syrup was spread and then 1 g was spread inside cap and bottle neck and the cap was again closed. Initial and 2 week observation for crystal growth of sucrose in the syrups at room temperature were monitored & results were recorded.

4. Result & Discussion

Physical test of syrup (See table 1):

<table>
<thead>
<tr>
<th>Test parameter</th>
<th>Sugar syrup (Control), Batch no. A 001</th>
<th>Partially inverted sugar syrup (Test), Batch no. A 002</th>
<th>Diphenhydramine HCl syrup prepared using sugar syrup (Control), Batch no: P 001</th>
<th>Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test), Batch no: P 002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>clear, pale yellow to brownish color</td>
<td>clear, pale yellow to brownish color</td>
<td>Clear, red color</td>
<td>Clear, red color</td>
</tr>
<tr>
<td>pH</td>
<td>5.2</td>
<td>3.5</td>
<td>5.1</td>
<td>5.12</td>
</tr>
</tbody>
</table>

Determination of content of invert sugars in sugar syrups(See table 2):

<table>
<thead>
<tr>
<th>Test parameter</th>
<th>Sugar syrup (Control), Batch no. A001</th>
<th>Partially inverted sugar syrup (Test), Batch no. A002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Content of invert sugars</td>
<td>10.2%</td>
<td>79.1%</td>
</tr>
</tbody>
</table>
4.1 Results of Experiment – A
Summary of the obtained results (See table 3):

<table>
<thead>
<tr>
<th>Observation Parameter</th>
<th>Sugar syrup (Control), Batch no. A 001</th>
<th>Partially inverted sugar syrup (Test), Batch no. A 002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal growth of sucrose</td>
<td>Presence of no crystal</td>
<td>Crystal of sucrose found</td>
</tr>
<tr>
<td></td>
<td>Zero time</td>
<td>Zero time</td>
</tr>
<tr>
<td></td>
<td>1 week</td>
<td>1 week</td>
</tr>
</tbody>
</table>

Table-3: Sugar syrup & partially inverted sugar syrup in opened Petri dish

Figure-1: Photos of sugar syrup & partially inverted sugar syrup in opened Petri dish (zero time and 1 week) at room temperature

Discussion: Theses above photos reveal that after 1 week, crystals of sucrose grow in the opened Petri dish of sugar syrup (batch no A001), which contained 10.2% of invert sugars. On the other hand, after 1 week, crystals do not grow in the opened Petri dish of partially inverted sugar syrup (batch no A002) that contained 79.1% of invert sugars. In sugar syrup, the % of content of sucrose is more, but in partially inverted sugar syrup, the % of content of sucrose is less and content of invert sugars are more. The invert sugars are more soluble than that of sucrose and have fewer tendencies to reform crystal structure when solvent evaporates. The more solubility and less tendency of invert sugars to reform crystal structure prevent the crystal formation[13].

4.2 Experiment - B
Summary of the result (See table 4 and Figure 2).

Table-4: Diphenhydramine HCl syrup prepared using sugar syrup & partially inverted sugar syrup kept in opened Petri dish

<table>
<thead>
<tr>
<th>Observation parameter</th>
<th>Diphenhydramine HCl syrup prepared using sugar syrup (Control), Batch no: P 001</th>
<th>Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test), Batch no: P 002</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zero time</td>
<td>Zero time</td>
</tr>
<tr>
<td></td>
<td>1 week</td>
<td>1 week</td>
</tr>
<tr>
<td>Crystal growth of sucrose</td>
<td>Presence of no Crystal</td>
<td>Crystal of sucrose Found</td>
</tr>
<tr>
<td></td>
<td>Zero time</td>
<td>Zero time</td>
</tr>
<tr>
<td></td>
<td>1 week</td>
<td>1 week</td>
</tr>
</tbody>
</table>
Diphenhydramine HCl syrup prepared using sugar syrup (Control) kept in opened Petri dish at zero time at room temperature, Batch no: P 001

Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test) kept in opened Petri dish at zero time at room temperature, Batch no: P 002

Diphenhydramine HCl syrup prepared using sugar syrup (Control) kept in opened Petri dish after 1 week at room temperature, Batch no: P 001

Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test) kept in opened Petri dish after 1 week at room temperature, Batch no: P 002

Figure-2: Photos of Diphenhydramine HCl prepared using sugar syrup & partially inverted sugar syrup in opened Petri dish (zero time and 1 week) at room temperature

Discussion: Theses above photos reveal that after 1 week, crystals of sucrose grow in the opened Petri dish of Diphenhydramine HCl syrup prepared using sugar syrup (Control). On the other hand, after 1 week, crystals do not grow in the opened Petri dish of Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test). In control sample, the % of content of sucrose is more, but in test sample, the % of content of sucrose is less & content of invert sugar is more. The invert sugars are more soluble than that of sucrose & have less tendency to reform crystal structure when solvent evaporates. The more solubility & less tendency of invert sugars to reform crystal structure prevent the crystal formation in Diphenhydramine HCl syrup[14].

4.3 Experiment – C

Summary of the result (See table 5 and Figure 3).

Table-5: Sugar syrup & partially inverted sugar syrup spread inside cap and on bottle neck

<table>
<thead>
<tr>
<th>Observation parameter</th>
<th>Filled bottle of Sugar syrup (Control), Batch no. P 001</th>
<th>Filled bottle of Partially inverted sugar syrup (Test), Batch no. P 002</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Zero time</td>
<td>2 weeks</td>
</tr>
<tr>
<td>Crystal growth of sucrose inside cap and on bottle neck</td>
<td>Presence of no Crystal</td>
<td>Crystal of sucrose found inside cap and on bottle neck</td>
</tr>
</tbody>
</table>
Sugar syrup (control) spread inside cap and on bottle neck observed at zero time at room temp, Batch no: A 001

Partially inverted Sugar syrup (test) spread inside cap & on bottle neck observed at zero time at room temp. Batch no: A 002

Sugar syrup (control) spread inside cap and on bottle neck observed after 2 weeks at room temp, Batch no: A 001

Partially inverted Sugar syrup (test) spread inside cap & on bottle neck observed after 2 weeks at room temp. Batch no: A 002

**Figure-3:** Photos of Sugar syrup & partially inverted sugar syrup spread inside cap and on bottle neck (zero time and 2 weeks) at room temperature

**Discussion:** Theses above photos reveal that after 2 weeks, crystals of sucrose grow inside cap & on bottle neck of sugar syrup (batch no A001) at room temperature[15]. On the other hand, after 2 weeks, crystals do not grow inside cap & on bottle neck of partially inverted sugar syrup (batch no A002) at room temperature. Sugar syrup (control sample) spread inside cap and on bottle neck results crystal of sucrose due to evaporation of water from the spread sugar syrup and also due to nature of crystal formation habit of sucrose. Partially inverted sugar syrup (test sample) spread inside cap and on bottle neck does not result crystal of sucrose even after evaporation of water from the spread syrup[16]. The crystal does not form, because in partially inverted sugar syrup, sucrose is converted into glucose and fructose and these invert sugars have more solubility and less tendency to form crystal[17].

**4.4 Experiment - D**

Summary of the result (See table 6 and Figure 4).

**Table-6: Diphenhydramine HCl prepared using sugar syrup & partially inverted sugar syrup spread inside cap and on bottle neck**

<table>
<thead>
<tr>
<th>Observation Parameter</th>
<th>Filled bottle of Diphenhydramine HCl syrup prepared using sugar syrup (Control), Batch no: P 001</th>
<th>Filled bottle of Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (Test), Batch no: P 002</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystal growth of sucrose inside cap and bottle neck</td>
<td>Presence of no Crystal</td>
<td>Crystal of sucrose found inside cap and on bottle neck</td>
</tr>
<tr>
<td>2 weeks</td>
<td>Presence of no Crystal</td>
<td>No crystal found inside cap and on bottle neck</td>
</tr>
</tbody>
</table>
Diphenhydramine HCl syrup prepared using sugar syrup (Control) observed at zero time at room temperature, batch no: P 001

Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (test) observed at zero time at room temperature, batch no: P 002

Diphenhydramine HCl syrup prepared using sugar syrup (Control) observed after 2 weeks at room temperature, batch no: P 001

Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (test) observed after 2 weeks at room temperature, batch no: P 002

**Figure 4:** Photos of Diphenhydramine HCl syrup prepared using sugar syrup & partially inverted sugar syrup spread inside cap and on bottle neck (zero time and 2 weeks) at room temperature

**Discussion:** Theses above photos reveal that after 2 weeks, crystals of sucrose grow inside cap & on bottle neck of Diphenhydramine HCl syrup prepared using sugar syrup (batch no P001) at room temperature. On the other hand[18], after 2 weeks, crystals do not grow inside cap & on bottle neck of Diphenhydramine HCl syrup prepared using partially inverted sugar syrup(batch no P002) at room temperature. Diphenhydramine HCl syrup prepared using sugar syrup (control sample) spread inside cap and on bottle neck results crystal of sucrose due to evaporation of water from the spread sugar syrup and also due to nature of crystal formation habit of sucrose. Diphenhydramine HCl syrup prepared using partially inverted sugar syrup (test sample)[19] spread inside cap and on bottle neck does not result crystal of sucrose even after evaporation of water from the spread syrup. The crystal does not form, because in partially inverted sugar syrup, sucrose is converted into glucose and fructose and these invert sugars have more solubility and less tendency to form crystal[20].

**5. Conclusion**

To reduce bitterness of drugs and to make palatable, sucrose is sometimes used at higher concentration. Normally sucrose remained dissolved in the solvent of product and does not form crystal[21].But when solvent of syrup product is evaporated on bottle neck, sucrose is crystallized and cap-locking of bottle happens[22].To prevent crystal on bottle neck of product, sugar syrup was processed using citric acid monohydrate, which partially hydrolyze sucrose into glucose and fructose. Glucose & fructose are more soluble than sucrose and their water activity is more than sucrose, that’s why invert sugars do not form crystal. Diphenhydramine HCl syrup was prepared using sugar syrup (control sample) and citric acid monohydrate treated sugar syrup (test sample)[23]. Both control and test sample were kept in opened Petri dish and spread inside cap and on bottle neck and found that
crystal resulted in control sample and did not result in test sample. So it can be concluded that filled bottle of product prepared using sugar syrup treated with citric acid monohydrate[24].

References