**Acetaminophen Sugar-free Syrup**

**WO2010/040652 A1**

**Formule :**

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| **N°** | **Constituants** | **Quantity (g)** |
| 1 | Acetaminophen | 2.40 |
| 2 | Polyethylene glycol | 16.00 |
| 3 | Citric acid | 0.25 |
| 4 | Sodium citrate | 0.51 |
| 5 | Potassium sorbate | 0.18 |
| 6 | Methyl paraben | 0.13 |
| 7 | Xanthan Gum | 0.40 |
| 8 | Glycerol | 10.00 |
| 9 | Sorbitol | 10.00 |
| 10 | Xylitol | 5.00 |
| 11 | Sucralose | 0.10 |
| 12 | Strawberry flavor | 0.12 |
| 13 | Mandarin flavor | 0.24 |
| 14 | Demineralized water | QS 100 ml |

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| **N°** | **Constituants** | **Quantity in g** | **Grade** | **Properties** |
| 1 | Acetaminophen | 2.40 |  | * Crystal form: Monoclinic type I. * Space group: P21/*n*. * pH in an aqueous solution: 5 - 6.5. * Solubility in water at 20°C: 1.4 g/100ml. |
| 2 | Polyethylene glycol (PEG) | 16.00 | PEG 6000 | * Solubilizing agent. * Density: 1.15- 1.21 g/cm3 at 25°C. * Viscosity: 200-270 mPa.s. * Surface tension: 55mN/m for a 10% w/v aqueous solution. |
| 3 | Citric acid | 0.25 |  | * Buffering agent. * Density: 1.665 g/cm3. * Solubility in water 133g/100ml at 20°C. * Viscosity: 6.5 mPa.s for a 50% w/v aqueous solution at 25°C. |
| 4 | Sodium citrate | 0.51 |  | * Buffering agent. * Monoclinic crystal. * pH: 7-9 in a 5% w/v aqueous solution * Density (bulk): 1.12 g/cm3. * Density (tapped): 0.99 g/cm3. * Density (true): 1.19 g/cm3. * Solubility: 1 in 1.5 of water. |
| 5 | Potassium sorbate | 0.18 |  | * Anti-oxidant preservative. * Density: 1.363 g/cm3. * Solubility in water at 20°C: 1 in 1.72. |
| 6 | Methyl paraben | 0.13 |  | * Anti-oxidant preservative. * Density (true): 1.352 g/cm3. * Solubility in water at 25°C: 1 in 400. |
| 7 | Xanthan gum | 0.40 | Xantural® 75 | * Thickening agent. * pH: 6-8 for a 1% w/v aqueous solution. * Viscosity: 1200-1600 for a 1% w/v aqueous solution at 25°C. * LOD:≤15% * Particle size: 75µm. |
| 8 | Glycerol | 10.00 |  | * Sweetening agent. * Density: 1.2656 at 15°C.   1.2636 at 2O°C.  1.2620 at 25°C.   * Surface tension: 63.4 mN/m at 20°C. * Viscosity in a 10% w/w aqueous solution at 20°C: 1.311 mPa.s. |
| 9 | Sorbitol | 10.00 |  | * Sweetening agent. * Liquid (non crystalling). * pH: 4.5 - 7 for a 10% w/v aqueous solution. * Density (bulk): 0.448 g/cm3. * Density (tapped): 0.400 g/cm3. * Density (true): 1.507 g/cm3. * Moisture content: >60% at 25°C. |
| 10 | Xylitol | 5.00 |  | * pH: 5-7 in a 50% w/v solution. * Solubility at 20°C in water: 1 in 1.6. * Mean particle size:0.6 -0.4 mm (milled grade 50µm) * Moisture content at 20°C and 52% relative humidity: 0.1% w/w. |
| 11 | Sucralose | 0.1 |  | * Sweetening agent. * pH: 5 – 6 for a 10% w/v aqueous solution at 20°C. * Density (bulk): 0.35 g/cm3. * Density (tapped): 0.62 g/cm3. * Density (true): 1.63 g/cm3. * Particle size distribution: 90%<12µm in size. * Viscosity: 0.6 – 3.8 mPa.s. |
| 12 | Strawberry flavor |  |  |  |
| 13 | Mandarin flavor |  |  |  |
| 14 | Demineralized water | QS 100 ml |  |  |

**Process:**

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| **Step** | **Description** | **Equipments** | **Parameters** |
| 1 | Demineralized water was heated. |  | Outlet temperature: 80°C. |
| 2 | Polyethylen glycol and methyl paraben were dissolved in the heated water. |  |  |
| 3 | The temperature of the resultant solution was lowered. |  | Outlet temperature: 60°C. |
| 4 | The potassium sorbate was added and dissolved. |  |  |
| 5 | The temperature of the resultant solution was lowered. |  | Outlet temperature: 40°C. |
| 6 | Paracetamol was added and dissolved |  |  |
| 7 | The temperature of the resultant solution was lowered. |  | Outlet temperature: 25°C. |
| 8 | Citric acid, sodium citrate, sucralose, xylitol, sorbitol and glycerol were added and dissolved. |  |  |
| 9 | The flavors and xanthan gum were then added to the clear solution and dissolved. |  |  |
| 10 | The final solution was made up to a volume of 100 ml with demineralized water |  | Water’s temperature: 25°C. |

**Syrup caracterestics:**

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| pH of the liquid excipient base | 4.5 - 6.5 |
| Viscosity at 25±3°C  (Measured with Brookfield viscometer spindle N°1 (LV1) at 40 RPM ) | 80- 140 cPs |