Volume-6, Issue-3, July-2015
Available Online at www.ijppronline.com
International Journal Of Pharma Professional's Research
Research Article

FORMULATION , EVALUATION AND STABILIZATION OF PARACETAMOL SYRUP

Vivek Kumar[*1], Achhrish Goel

1. Morepen Laboratories Limited, Parwanoo, Himachal Pradesh

ISSN NO:0976-6723

Abstract

In Liquid oral formulation, the stability of the active and inactive ingredients is of major issue for the formulator. Usually active ingredients are less stable in aqueous formulation than in solid dosage form. Hence it is important to stabilize and preserve the liquid oral formulation which contains water. In this paper we formulate stabilized Paracetamol syrup. Paracetamol is an analgesic, antipyretic and anti-inflammatory drug. The syrup was evaluated with respect to appearance, pH, taste and assay.

Keywords: - Paracetamol, Syrup, Stabilized, Freeze and thaw studies.

Introduction

Liquid oral formulations are generally syrups, solutions, emulsions or suspensions which have one or more active ingredients in a suitable vehicle. Some of the oral liquid formulations are prepared by dilution of concentrated liquid preparations for oral drops or syrups in a suitable vehicle. [1] Syrups are aqueous formulations with sweet taste and suitable viscosity. The aceptable sweet taste can be obtained by using a appropriate combination of polyols, sweetening agents with aromatic and flavouring agents.[2] Paracetamol (Acetaminophen) is a well-known ,widely used and easly available over the counter (OTC) molecule having analgesic, antipyretic and weak anti-inflamatory action. It is used in the severe pain caused by advanced cancers.[3,4,5] and also in the treatment of arthritic and rheumatic conditions involving muscular and joint pain and in other painful disorders such as headache, dysmenorrhoea, myalgia and neuralgia. Its IUPAC name is 4-Hydroxyacetanilide having chemical formula C8H9NO2 [6].

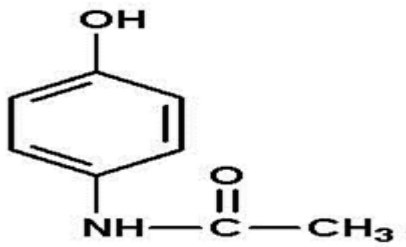

Figure no.1 Structure of Paracetamol

Material And Methods: -

Paracetamol was received as a gift sample from Total heathcare. Other excipients namely Sodium methyl paraben, Sodium propyl paraben, Bronopol, Sodium saccharin, Aspartame, citric acid, menthol were purchased from S.D. Fine chemicals limited, Mumbai. All the chemicals used were of analytical grades.

Formulation Of Syrup: -

Three different trials were planned to develop the formulation. In this Base (Sorbitol, sugar and Glycerin and Propylene glycol, Polyethylene glycol-400 as solublizer) were used in different concentration to develop the formulation and it is shown in table no 1**.**

Use of Excipients: -

Different types of excipients were used for the development so their used explained down in the table no 2.

Procedure: -

Firstly Sugar base was prepared with boiled water and then all the preservatives were dissolved in boiled and cooled water added into the sugar base. Now Paracetamol was dissolved in Propylene glycol at 400C-500C. After that Glycerine and Sorbitol were added and then sweetening, colouring and flavouring agent were added. Menthol was also dissolved in Propylene glycol. The final pH i.e. between 5.5-6.5 was adjusted with citric acid. Now volume was maked with boiled and cooled water.

Table no 1: - Three different trails of Formulation

S.NO	INGREDIENTS	F1	F2	F3
1	Paracetamol	26.40	26.40	26.40
2	Propylene glycol	250.00	50.00	0.00
3	Polyethylene glycol 400	0.00	0.00	100.00
4	Sodium methyl paraben	1.00	1.00	1.00
5	Sodium propyl paraben	0.10	0.10	0.10
6	Bronopol	0.10	0.10	0.10
7	Sodium saccharin	1.00	1.00	0.00
8	Aspartame	0.50	0.00	1.00
9	Sorbitol	100.00	100.00	100.00
10	Sugar	350.00	350.00	350.00
11	Glycerine	100.00	100.00	100.00
12	Citric acid	3.00	3.00	3.00
13	Flavour raspberry	3.00	3.00	3.00
14	Colour Ponceau 4R	0.03	0.03	0.03
15	Menthol	0.20	0.20	0.20

Table No 2: - Use of excipients.

S.NO	INGREDIENTS	USE
1.	Paracetamol	Active
2.	Propylene glycol	Solublizer
3.	Polyethylene glycol 400	Solublizer
4.	Sodium methyl paraben	Preservative
5.	Sodium propyl paraben	Preservative
6.	Bronopol	Preservative
7.	Sodium saccharin	Sweetening Agent
8.	Aspartame	Sweetening Agent
9.	Sorbitol	Stablizer
10.	Sugar	Base
11.	Glycerine	Stabilizer
12.	Citric acid	Acidifier
13.	Flavour raspberry	Flavoring Agent
14.	Colour Ponceau 4R	Coloring Agent
15.	Menthol	Soothing agent

Evaluation of Syrup: - [8,9]

1.Determination of pH

The pH value conventionally represents the acidity or alkalinity of an aqueous solution. The pH value of a solution was determined potentiometrically by means of glass electrode. A digital pH meter was allowed to stabilize. Then the pH meter was standardized using buffer tablets. The suspension formulation was placed in the pH meter. The reading was noted when there is no fluctuation in the pH meter.

2.Determination of Weight per ml

A pre weighed 50 ml volumetric flask was taken and the oral syrup was added up to the mark. The net volume was noted. Then weighed the above volumetric flask to evaluate weight per ml. Calculated the density accordingly.

3.Accelerated stability study

F1 syrup was packed in 100 ml Pet bottle. The packed bottles were placed in stability chamber maintained at 40 + 2 °C and 75 + 5% RH for 3 month. Samples were collected at days 0, 30, 60 and 90. The analyses comprised chemical testing of quantifiable parameters, which could possibly change during storage, such as pH, drug contents, colour, taste, odour and drug release.

4.Freeze and thaw studies

The Freeze and Thaw studies were done by exposing the final formulation (F1) alternately at 40C and 400C. There was no precipitation and turbidity observed in the formulation.

Results: -

1. Evaluation of Syrup: -

Evaluation of Syrup was carried out for various parameters like confirmation of formation of precipitation, pH, odor, and taste, and assay.

Table no 3: - Evaluation of syrup on the basis of different parameters.

S.NO	PARAMETERS	F1	F2	F3
1.	Colour	Red colour	Red colour	Red colour
2.	Appearance	Clear Solution	Turbid solution	Clear Solution
3.	Odour	Raspberry	Raspberry	Raspberry
4.	Taste	Sweet	Sweet	Sweet
5.	pH	6.0	5.9	6.2
6.	Assay	100.24	99.97	100.10

Accelerated Stability Studies: -

Table no 4: - Data of stability studies for Final Formulation (F1)

S.NO	PARAMETERS	INITIALS	TIME PERIODS		
			1 MONTH	2 MONTH	3 MONTH
1.	Colour	Red colour	Red colour	Red colour	Red colour
2.	Appearance	Clear Solution	Clear Solution	Clear Solution	Clear Solution
3.	Odour	Raspberry	Raspberry	Raspberry	Raspberry
4.	Taste	Sweet	Sweet	Sweet	Sweet
5.	pH	6.0	6.0	5.9	5.8
6.	Assay	100.24	100.11	100.03	99.95

Freeze and thaw studies:-

There was no precipitation and turbidity observed in the final formulation.

Conclusion: -

The three trials were planned to prepare this formulation with excipients in different quantity like Propylene glycol used as solublizer, Sodium saccharine as sweetner. We found that the first formulation (F1) i.e. final formulation was clear and stabilized. In the second (F2) formulation crystallization was observed due to less quantity of propylene glycol and the third (F3) formulation was not of good taste. So, it was concluded that F1 formulation was good and stabilized formulation.

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Correspondence Address:
Vivek Kumar
Research Scientist,
Morepen Laboratories Limited, Himachal Pradesh
E-mail- vivek21288@gmail.com
Phone: +919466656013