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Research

Formulation and Evaluation of Praziquantel Tablets (600 Mg)

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Abstract

The aim of this study is to develop immediate release praziquantel tablets with the use of sodium Lauryl sulphate as it's main function as a solubility enhancer and croscarmellose sodium as a super disintegrants. Formulation is carried out by wet granulation procedure and followed with post evaluation studies which include, Weight variation test, Hardness test, friability test, disintegration test and dissolution test.The relative dissolution study was performed in diverse media, with and without the utilization of the surfactant. The summary results show that the test product (Praziquantel tablets 600mg) is comparable to reference product(Biltricide tablets 600mg), Since the F1 and F2 values are found to be within limits. All the physical and chemical parameters are found competent and lined -up to the quality target product profile.

Keywords: Sodium lauryl suphate, croscarmellose sodium, wet granulation, Critical process parameters, Critical Quality Attributes, Quality By Design

INTRODUCTION

The BCS (Biopharmaceutics Classification System)-based biowaiver approach is intended to reduce the need for in vivo bioequivalence studies i.e., It can provide a surrogate for in vivo bioequivalence. In vivo bioequivalence studies may be exempted if an assumption of equivalence in in vivo performance can be justified by satisfactory in vitro data. The BCS is a scientific approach based on the aqueous solubility and intestinal permeability characteristics of the drug substance.

A drug substance is classified as highly soluble if the highest single therapeutic dose is completely soluble in 250 ml or less of aqueous media over the pH range of 1.2–6.8 at 37±1°C. In cases where the highest single therapeutic dose does not meet this criterion but the highest strength of the reference product is soluble under the aforementioned conditions, additional data should be submitted to justify the BCS-based biowaiver approach.

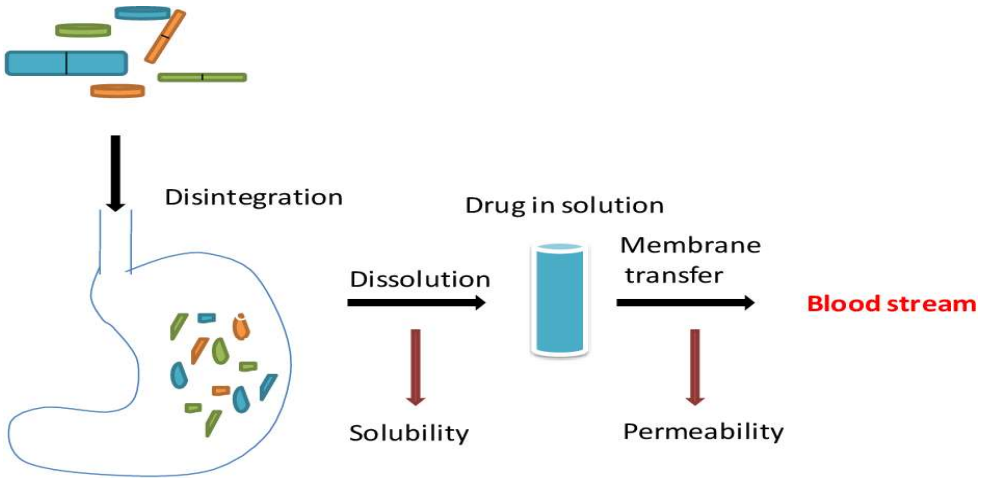
The sponsor is expected to establish experimentally the solubility of the drug substance over the pH range of 1.2–6.8 at 37±1ºC. At least three pH's within this range, including buffers at pH 1.2, 4.5 and 6.8, should be evaluated. In addition, solubility at the pH of lowest solubility of the drug substance should be evaluated if it is within the specified pH range. These experiments should demonstrate that solubility is maintained over relevant timeframes to accommodate the expected

Permeability: The assessment of permeability should preferentially be based on the extent of absorption derived from human pharmacokinetic studies, e.g., absolute bioavailability or mass balance.

Drug Substance Stability in the Gastrointestinal Tract

BCS	High solubility	Low solubility
High permeability	**CLASS I**	**CLASS II**
Low permeability	**CLASS III**	**CLASS IV**

Class I:- High solubility, High permeability – Well absorbed compounds. Class II:- Low solubility, High permeability – Dissolution rate-limited absorption. Class III:- High olubility, Low permeability – Permeability-limited absorption. Class IV:- Low solubility, Low permeability – Poorly absorbed compounds. Solubility, dissolution and permeability are the key factors for determining the optimal therapeutic effect of the drugs at the target site.



Helminths: Helminths are parasitic worms that can infect humans and other animals. There are three types of helminths: flukes (trematodes), tapeworms (cestodes), and roundworms (nematodes).Types Of Helminths**:** Roundworms**:** Flukes**:-** Tapeworms**:-** Thorny-headed worms

Anti- Helminthics: Praziquantel drug. Praziquantel drug is used to treat Schistosoma and Liver fluke. Praziquantel drug will increase in future either administered alone or along with other anti- helminthics.

Design of Experiment (DoE): Design of Experiment (DoE) is a systematic and statistical method used to plan,conduct, analyze, and interpret controlled tests to evaluate the factors that may influence a particular outcome or process. DoE aims to identify cause-and-effect relationships and optimize processes by systematically varying the input variables and analyzing their effects on the output.

Key Objectives:Optimization: Identify the optimal conditions for a process or product.

Understanding Relationships: Determine the relationship between factors and responses.

Efficiency: Reduce the number of experiments needed by systematically exploring multiple factors simultaneously.

Robustness: Develop processes that are less sensitive to variations in inputs and external conditions.

Types of Experimental Designs

Full Factorial Design: Studies all possible combinations of factors and levels.Suitable for a small number of factors.Provides complete information about main effects and interactions.

Fractional Factorial Design: Studies a subset of all possible combinations.Reduces the number of experiments needed.Suitable for preliminary screening when there are many factors.

Response Surface Methodology (RSM): Used to model and optimize processes.Helps identify optimal conditions within the design space.Includes designs like Central Composite Design (CCD) and Box-Behnken Design.
Taguchi Methods: Focus on robust design and improving quality.Uses orthogonal arrays to study a large number of variables with a smaller number of experiments.Emphasizes minimizing variability and improving performance.

AIM & OBJECTIVES

The primary aim of this project is to develop and optimize a robust formulation for 600 mg praziquantel tablets using the Quality by Design (QbD) approach. This includes ensuring blend uniformity and achieving desired dissolution profiles to enhance therapeutic efficacy and patient compliance.

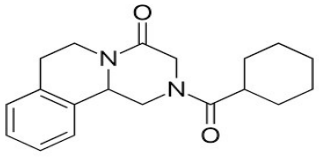
Formulation Development

To design and develop a formulation for 600 mg praziquantel tablets that ensures optimal bioavailability and patient acceptability.To select appropriate excipients and optimize their concentrations to achieve desired physical and chemical properties.

MATERIALS AND METHODS

Praziquantel, Microcrystalline cellulose PH 101, Maize starch Croscarmellose sodium Sodium lauryl sulphate Povidone K- 30 Isopropyl alcohol, Methylene chloride Magnesium stearate Hydroxy propyl methyl cellulose E15 Titanium dioxide, Propylene glycol, Sifter
Equipment: Rapid Mixture granulator 1000 l, Fluid Bed Dryer Multimill Octagonal blender Analytical balance Moisture analyzer Bulk density apparatus.

DRUG PROFILE:
Praziquantel



General Information: Brand Names: Bactericide, Distocide, **Molecular Formula:** C19H24N2O2, **Molecular Weight:** 312.41 g/mol.
Indications: Praziquantel is an anthelmintic medication primarily used for the treatment of parasitic worm infections. It is effective against a variety of trematodes (flukes) and cestodes (tapeworms).
Recent Research and Developments: Studies continue to explore improved formulations and combination therapies to enhance the efficacy and reduce the side effects of praziquantel, particularly in pediatric populations.
Manufacturing process: Following steps are involves in the manufacturing process involving Sifting, Dry Mixing, Paste preparation and Granulation, Drying, Milling, Lubrication, Compression, Coating.
Methods for the Quality Target Profile Praziquantel tablets 600 mg: In grouping combination with other additional antiretroviral agents, Praziquantel 400 mg t extended release Tablets are indicated as an alternative for treatment of HIV-1 infection. A brief explanation about quality characteristics that affects formulation of Praziquantel ER Tablets is given in Table 1.

Representation of the in process test during the formulation and manufacturing of the product

Sr.No	Test	Methods
Granulation :		
1.	Loss of Drying	Performed in moisture analyzer balance
2.	Bulk density	Measurement of Bulk density was done by pouring powder into a measuring cylinder through sieve # 20 and the initial weight was noted. The initial volume was termed as bulk volume.11
3.	Tapped density	Tapped density is defined as the ratio between aggregate weights of granules to the tapped volume of powder. Measurement of the volume was done by tapping the granules 750 times. If the variance in volume exceeds 2%, further tapping should be done for 1250 times. It was conveyed in g/ml
4.	Angle of Repose	Angle of repose was done by using powder flow tester. Angle of repose can be

Sr.No	Test	Methods
		calculated by measuring the height and radius of the pile of granules
5.	Compressibility index	It demonstrates the flow properties of the granules. It is conveyed in the form of % and can be calculated using bulk density and tapped density.
6.	Hausner Ratio	Hausner ratio is an indirect way of accessing the ease of granules flow. It can be calculated by using bulk density and tapped density
Compression		
7.	Weight Variation	Randomly 20 tablets were selected and weighed using a single balance. Standard deviations were calculated and checked with the standard pharmacopeial limits.
8.	Thickness	Tablets were selected randomly from all batches and measurement of thickness was done by using Vernier Calliper.1
9.	Hardness	The strength of tablet is expressed in the form of tensile strength (Kg/cm2). The amount of force required to break the tablets was measured by using a hardness tester
10.	Friability	Randomly 20 tablets were selected and weighed from all the batches. The weighed tablets then placed in friabilator and then ran for 100 revolutions. After completion of 100 revolutions tablets were de-dusted, re-weighed and %friability was calculated.

Compare the amount of praziquantel dissolved at each time point to the specifications provided by the relevant pharmacopeia.Typically; a certain percentage of the labeled amount of praziquantel (e.g., not less than 75% of the labeled amount) should dissolve

RESULTS AND DISCUSSION

Different Trail were taken for the optimizing the formula same has been determined in table 1 Different quantity of ingredient were changed for the formulation to optimize the formula.

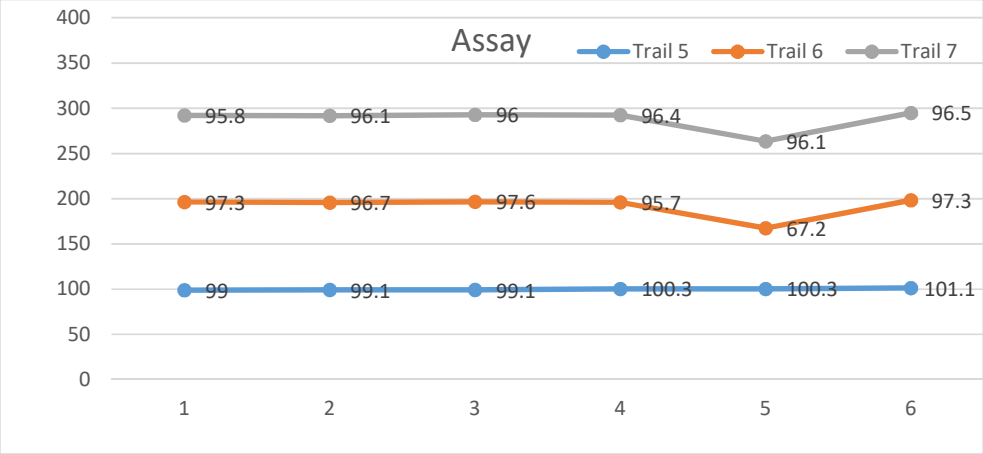
Table 1 : Different quantity of ingredient were changed for the formulation to optimize the formula

Ingredient	**Quantity in batch per kg (mg/Tablets)**						
	Trail 1	**Trail 2**	**Trail 3**	**Trail 4**	**Trail 5**	**Trail 6**	**Trail 7**
Praziquantel	600.0	600.0	600.0	600.0	600.0	600.0	600.0
Microcrystallin cellulose PH 101	**66.50**	66.50	66.50	**78.50**	**81.50**	81.50	**66.50**
Maize starch	**65.00**	65.00	65.00	65.00	65.00	65.00	**65.00**
Crospovidone	100.00	100.00	**NA**	NA	NA	NA	100.00
Croscarmellose sodium	**NA**	**NA**	**100.**00	100.00	100.00	100.00	**NA**
Sodium lauryl sulfate	**20.00**	20.00	20.00	**18.00**	**15.00**	15.00	**20.00**
Povidone k 30	20.00	20.00	20.00	**25.00**	25.00	25.00	20.00
Purified Water	QS	QS	QS	QS	QS	QS	QS
Sodium lauryl sulfate(paste)	**NA**	**NA**	**NA**	**NA**	**NA**	NA	**NA**
Crospovidone	**30.00**	30.00	NA	NA	NA	NA	**30.00**
Croscarmellose sodium	**NA**	**NA**	30.00	**15.00**	15.00	15.00	**NA**
Magnesium stearate	8.5	8.5	8.5	8.5	8.5	8.5	8.5
Total	**910.0**	**910.0**	**910.0**	**910.0**	**910.0**	**910.0**	**910.0**
Hydroxy Propyl Methyl cellulose E5	9.50	NA	NA	NA	NA	NA	NA
Hydroxy Propyl Methyl cellulose E15	0.950	**11.5**	11.5	11.5	11.5	11.5	11.5
Titanium dioxide	6.55	4.75	4.75	4.75	4.75	4.75	4.75
Propylene glycol	3.0	3.75	3.75	3.75	3.75	3.75	3.75
Isopropyl alcohol	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Methylene Chloride	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total	**930.0**	**930.0**	**930.0**	**930.0**	**930.0**	**930.0**	**930.0**
Flow Properties	Very Poor	Poor	Passable	Fair	Good	Excellent	Excellent

Conclusion : From the above table all in process control and parameter is observed well within criteria for Trail batches Trail 6 and Trail 7.

Assay of Tablets

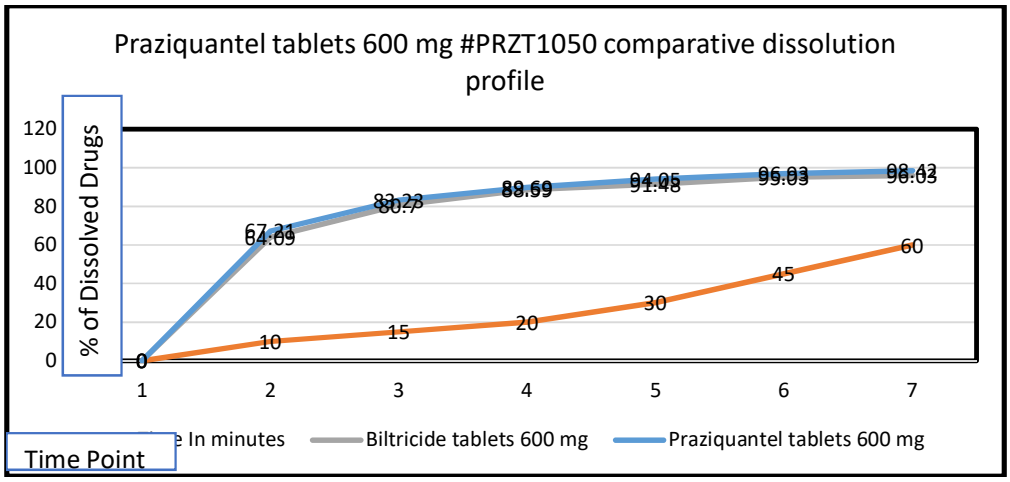
Assay	Trail 5	Trail 6	Trail 7
1	99.0	97.3	95.8
2	99.1	96.7	96.1
3	99.1	97.6	96.0
4	100.3	95.7	96.4
5	100.3	67.2	96.1
6	101.1	97.3	96.5
Mean	100	96.7	96.2
SD	**1.13**	**0.84**	**0.26**
%RSD	**1.13**	**0.87**	**0.27**
HPLC	QC-HPLC00	QC-HPLC001	QC-HPLC001
Column	QC-COL-005	QC-COL-005	QC-COL-005



Comparative dissolution profile of lab Scale up batch: Praziquantel tablets 600 mg #PRZT1050 comparative dissolution profile (Trial 11).

Dissolution Medium: 0.1 N Hydrochloride acid + 0.2 % SLS

Sr/No	Time point	Biltricide	Test Sample	(Rt-Tt)	(Rt-Tt) X (Rt-Tt)	(Rt-Tt)	(Rt)
0	0	0.00	0.00	0.00	0.00	0.00	0.00
1	10	64.09	69.59	-5.51	30.33	5.51	64.09
2	15	80.70	84.32	-.362	30.11	3.62	80.70
3	20	88.59	92.67	-4.08	16.64	4.08	88.59
4	30	91.48	97.78	-6.30	39.63	6.30	91.48
5	45	95.03	100.96	-5.93	35.18	5.93	95.03
6	60	96.02	100.54	-4.52	20.45	4.52	96.02
			SUM		155.34	29.96	515.91
		{SQ[Rt-Tt]}/n			25.8900		
		1 + {SQ[Rt-Tt]}/n			26.8900		
		SQRT (1 + {SQ[Rt-Tt]}/n)			5.1856		
		100/SQRT (1 + n/{SQ[Rt-Tt]})			19.2843		
		LOG100/SQRT (1 + n/{SQ[Rt-Tt]})			1.2852		
		Similarity factor(F2)			**64.26**		
		Difference Factor (F1)			**5.81**		



The comparative dissolution profile study was performed in different media, with and without surfactant.The summary results show that the test product (Praziquantel tablets 600mg) is comparable to Reference product Biltricide tablets 600mg), since the F1 and F2 values are found to be within limits

CONCLUSION

This study shows that the dissolution rate of Praziquantel tablets 600mg can be enhanced. Sodium Lauryl Sulphate is used as a solubility enhancer and crosmellose sodium is used as a Dis integrant The comparative dissolution profile study was performed in different media, with and without surfactant. The summary results show that the test product (Praziquantel tablets 600mg) is comparable to Reference product Biltricide tablets 600mg), since the F1 and F2 values are found to be within limits. The formulated Praziquantel product has shown better release kinetics when compared to reference product Biltricide. All the physical and chemical parameters are found satisfactory and aligned to quality target product profile. Hence these quantities of API and are optimized for the formulation. The study meets the specification criteria.It is observed that Praziquantel tablets which are formulated shows maximum efficiency at 45 minutes.The drug gets completely dissolved at 45 minutes.Treating efficiency is increased as the drug reaches the target site quickly and starts working quickly, showing the quick relief from the symptoms.

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