DEVELOPMENT AND EVALUATION OF PRAZIQUANTEL LEADED CHEWABLE TABLET FOR TREATMENT OF HELMINTHIASIS

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Abstract

Nearly a billion people are affected with helminthiasis, a category of parasitic illnesses caused by different worms, mostly in developing countries with inadequate sanitation and hygiene. These infections may have long-term impacts on the physical and cognitive development of children and induce symptoms such as abdominal discomfort, diarrhea, anemia, and malnutrition. Despite the fact that helminthiasis may be treated with anthelmintic drugs such as albendazole, mebendazole, and praziquantel, its prevention needs a multidisciplinary strategy that includes better sanitation, hygiene, and health education. Chewable tablets are advantageous for those who have difficulties swallowing pills or capsules since they may be chewed before ingesting, giving them a more convenient and appetizing treatment alternative. They are available in grape, cherry, and orange tastes, which may encourage patients to take their drugs more often and lower the chance of adverse reactions. Chewable praziquantel tablets may be more successful than regular tablets or capsules in treating parasitic illnesses such as schistosomiasis and tapeworms. Chewable praziquantel tablets have been proven to have a greater bioavailability and quicker absorption rate than regular pills, resulting in better treatment results. In order to improve medication compliance and treatment success for parasitic infection, we have designed and evaluated chewable praziquantel tablets using direct compression method.

Keywords: Chewable tablets, Helminthiasis, praziquantel, Super disintegrate,

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1. Introduction

Helminthiasis is a category of parasitic illnesses caused by worms, including nematodes, trematodes, and cestodes, which affects over one billion people globally. Most of these infections happen in developing countries, where sanitation and hygiene are often not very good. The most frequent kinds of helminthiasis are soil-transmitted helminths (STHs), schistosomiasis, and lymphatic filariasis. These diseases cause stomach pain, diarrhea, anemia, and poor nutrition, among other things. Helminthiasis can impair children's physical development and cognitive growth, leading to long-term consequences(*Helminth Control in School-Age Children : A Guide for Managers of Control Programmes*, n.d.; Hotez et al., 2005). Moreover, it can increase the risk of other illnesses like tuberculosis and HIV. Drugs like albendazole, mebendazole, and praziquantel, which are called "anthelmintics," are used to treat helminthiasis. But the prevention of helminthiasis requires a multidisciplinary approach, including improved sanitation, hygiene, and health education. Anthelmintic drugs can be challenging, as reinfection can occur due to poor sanitation and hygiene. Therefore, a multidisciplinary approach is necessary to prevent helminthiasis(Hotez et al., 2004, 2005; King et al., 2005).

Chewable tablets are a medicine that is meant to be chewed before swallowing. They are usually given to kids or people who have trouble swallowing pills. Although the medication's formulation may be slightly altered to accommodate the chewable form, the active ingredients in chewable tablets are the same as those in traditional tablets or capsules. Tablets that can be chewed come in flavors like grape, cherry, or orange, which makes them more palatable and easier to swallow. When taking chewable tablets, following the directions on the label or from your healthcare provider is critical. Some medicines may be more effective with food or water, while others may be more effective when taken on an empty stomach. Enjoyable tablets give a practical and simple to-involve choice for individuals who experience issues gulping customary tablets or cases.(Bhattacharjee et al., 2017; Dasankoppa et al., 2017; Kimaro et al., 2019; Nyamweya, 2020)

People who are infected with parasitic infections like schistosomiasis and tapeworms should have access to praziquantel via a tablet that can be chewed to have a treatment option that is both more convenient and more appealing. Tablets that can be chewed are less difficult to swallow and come in a variety of flavors, both of which have the potential to increase medication adherence and lower the likelihood of adverse effects. Additionally, chewable tablets may be more effective than traditional tablets or capsules at treating parasitic infections. Studies have demonstrated that chewable praziquantel tablets have a higher bio-availability and a faster absorption rate (Keiser et al., 2009; Tarning et al., 2012). On this aspect, we have prepared to develop and evaluate praziquantel chewable tablets using the direct compression process.

2. Materials And Methods

Materials: Praziquantel obtained from sodium starch glycolate, mannitol, sodium lauryl sulphate, PVP K30, magnesium stearate, talc, and HCl. All the chemicals used are obtained from SRL Chemicals Pvt. Ltd (Chennai, INDIA).

Methods:

Calibration of Praziquantel:

100mg of the crude drug is taken and dissolved using 100ml of methanol for standard stock solution. The stock solutions are diluted as 2µg/ml, 4µg/ml, 6µg/ml, 8µg/ml, and 10µg/ml. These concentrations are scanned in UV Spectroscopy for the measurement of absorbance.

Preformulation studies:

Bulk density:

The bulk density is measured by gently filling a blend of 25g in a 100-measuring cylinder. The measurement of the filling is noted and taken as bulk volume. Bulk density is calculated using the following formula

Bulk density = Powder weight (g) / Bulk volume (ml)

Tapped density:

The tapped density is measured by taking 25g of blend in a 100-measuring cylinder and tapping the cylinder for 1-2mins. Then the measurement in the cylinder is noted and taken as tapped volume. The tapped density is determined using the following formula.

Tapped density= Powder weight (g) / Tapped volume (ml)

Carr's index:

It is also known as the compressibility index, which influences the particle size, cohesiveness, and flow rate. It is derived from tapped density and bulk density. Carr's index is calculated using the following formula

%Carr's index = (Tapped density – Bulk density) / Tapped density × 100

Hausner's ratio:
Hausner's ratio is used to determine the flow property of the sample. It is calculated using the following formula

Hausner's ratio = Tapped density / Bulk density

Angle of repose:
The angle of repose is for measuring frictional force, which is calculated using the funnel and stand method. In an experiment, a funnel was set up with its mouth positioned 3cm above the base. A blend weighing 10g was placed on the funnel's mouth and allowed to pour onto the base. The resulting pile's height and radius were measured to determine the angle of repose using a formula.

Angle of repose (θ) = $\tan^{-1}$ (h/r),
h = height of the pile, r = radius of the pile.

Fourier transform infrared spectroscopy:
The interaction between the excipients and combination of blend is investigated by FTIR using KBr technique. The samples are dispersed in the KBr and examined for the functional groups range from the FTIR band, which is scanned in the range of 4000 to 400 cm^{-1}. (Dahiya et al., 2015; Jagdale et al., 2010; Landsberg et al., 2008; Mehmood Yasir et al., 2015; Sharma, Kuchi Shishir Chandra, Y. Kranthi Kumar, 2014; Simpson et al., 2007)

Preparation of praziquantel chewable tablet:
The chewable tablet is prepared by direct compression method. In the preparation, PVP k30 is used as binder, mannitol is used as sweetening agent, sodium starch glycolate is used as disintegrant, magnesium stearate is used as lubricant and talc is used as glidant. All the ingredients are measured according to the formula table (table no. 1) except talc and magnesium stearate all the ingredients are passed through sieve #40, then the glidant and lubricant is added and the blend is subject for punching using multi tool 8 station rotating machine with high compression capacity.

Table 1: Formulation tablet for Praziquantel chewable tablet

Ingredients	F1	F2	F3	F4	F5	F6
Praziquantel	150	150	150	150	150	150
PVP k30	25	23	21	19	17	15
Sodium starch glycolate	15	17	19	21	23	25
Mannitol	170	170	170	170	170	170
Sodium lauryl sulphate	15	15	15	15	15	151
Magnesium stearate	10	10	10	10	10	10
Talc	5	5	5	5	5	5

Post compression evaluation parameters:
General appearance: the tablets were checked for the colour, shape and it must be free from cracking and chipping.
Hardness test: The hardness of the tablets varies depends on the type of tablet. 4-12 kg/cm2 is the allowable limit for continuous release tablets. A Pfizer hardness tester was used to determine the hardness. The research was carried out on a total of five replicates.
Weight variation: Twenty tablets were measured individually. The average weight was calculated using the total weight of all tablets. The individuals' weights were compared to the average weight. The weight variance percentage difference should be below the permissible range. The weight variance is calculated using the following formula:

% deviation = individual weight - average weight / average weight × 100

Friability: For the friability testing 10 tablets were taken and weight collectively then placed together in the friability chamber. The tablets are allowed to roll due to free fall inside the chamber for 4 mins. Then the tablets are collected from the friability chamber and weight again. The permissible range of friability test is 1.0% and it is calculated using the formula:

$$\% F = (w1 - w2) / w1 \times 100$$

Invitro dissolution study: Praziquantel chewable tablets are subjected to in vitro dissolution using USP paddle type 2 apparatus. The bowl is filled with 900ml of 0.1N HCl at 37℃. This experiment is carried out for 1 hours. 5ml sample is withdrawn at frequent intervals such as 5, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60mins and replaced with buffer solution. The absorbance of the withdrawn samples is estimated using UV Spectroscopy at 218nm and the percentage cumulative drug release is calculated.

3. Results and Discussion

Calibration curve of praziquantel:

Table 2 displays the absorbance measurements, while Figure 1 illustrates the calibration curve for praziquantel. To prepare the standard stock solution, take 100mg of praziquantel and transfer it into a 100ml volumetric flask. Add a small amount of methanol and shake it until the drug dissolves, then make it up to 100ml with methanol. The stock solution can be diluted with methanol to produce concentrations of 2, 4, 6, 8, and 10µg/ml, which can be measured using ultraviolet spectroscopy to determine the absorbance at specific nm. The absorbance was found to be linear at 218 nm, with a regression value of 0.9966.

Table 2: Absorbance value of Praziquantel

Concentration (µg/ml)	Absorbance at 218nm
0	0
2	0.09
4	0.149
6	0.215
8	0.296
10	0.354

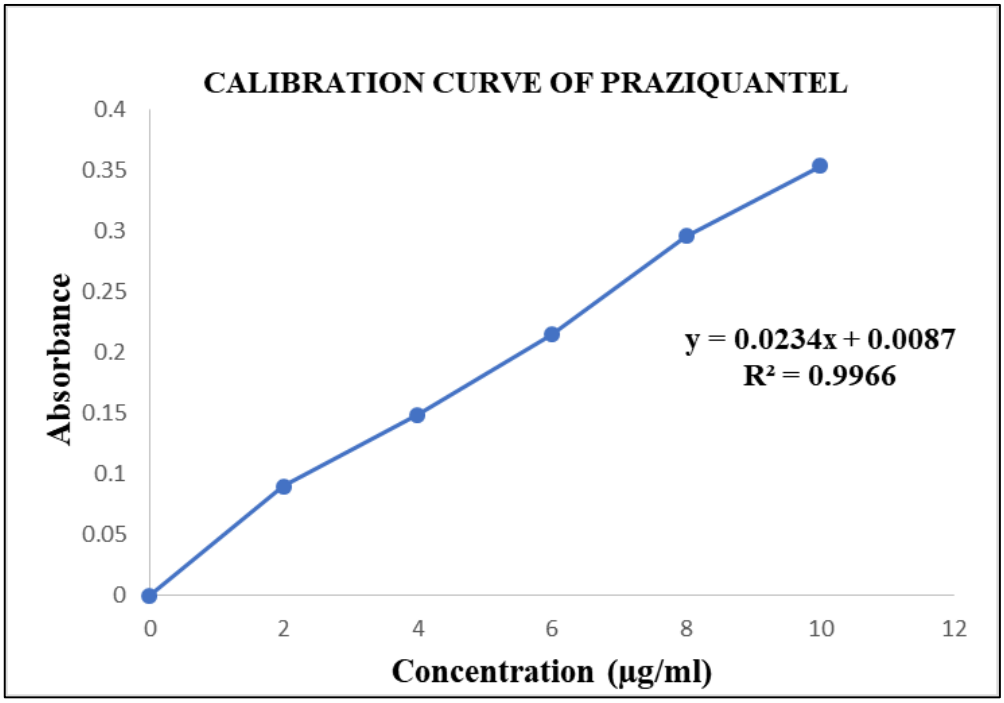

Figure 1: Calibration curve of praziquantel

Preformulation studies

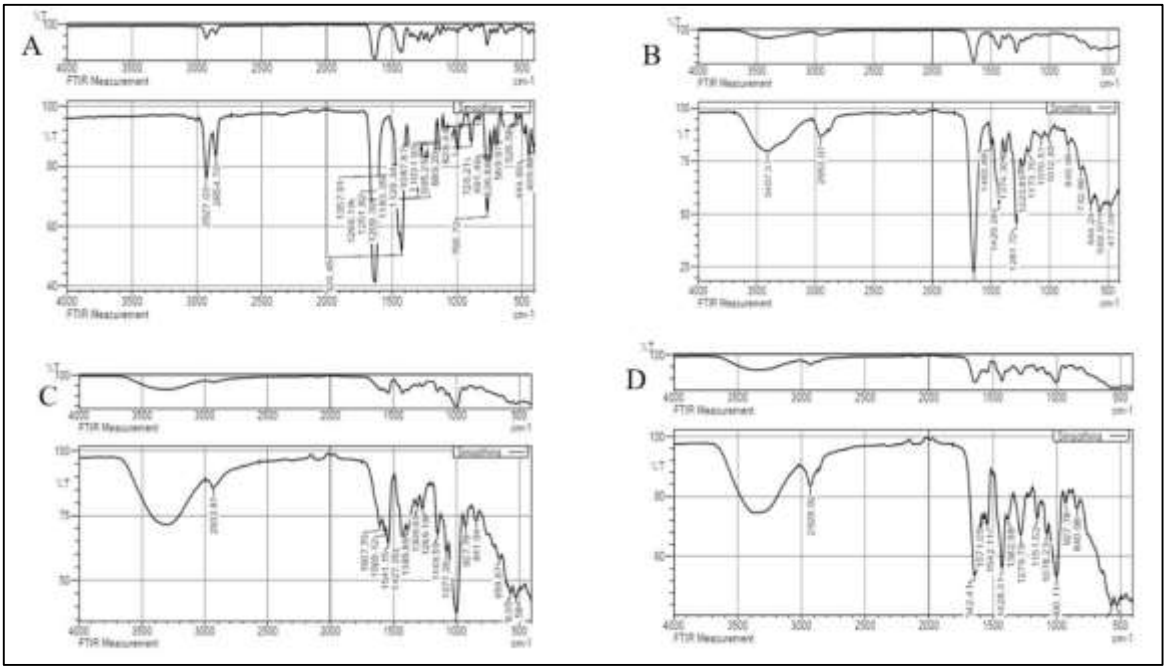

Figure 2: FTIR graph of a) Drug, b) PVP k30, c) Sodium starch glycolate , d) Mixture of drug and excipients

FTIR is a typical analytical method used to explore the interactions between medicines and other excipients in a formulation. In this instance, the FTIR analysis did not reveal any significant interactions between the medicine and formulation excipients. This indicates that the stability and effectiveness of the medicine are not impacted by the excipients and that the excipients are compatible with the drug (figure 2).

Table 3: Preformulation parameter of Chewable tablet

Formula	Bulk density	Tapped density	Carr's index	Hausner's ratio	Angle of repose	Flowability
F1	0.75 ± 0.01	0.8 ± 0.01	5 ±0.7	1.04 ± 0.03	28.7 ± 1.09	Excellent
F2	0.70 ± 0.00	0.73 ± 0.02	2.7 ± 0.7	1.06 ± 0.07	26.5 ± 0.08	Excellent
F3	0.67 ± 0.02	0.69 ± 0.04	4.6 ± 0.8	1.08 ± 0.04	29 ± 0.06	Excellent
F4	0.72 ± 0.03	0.76 ± 0.01	4.1 ± 0.9	1.03 ± 0.02	26.9 ± 0.09	Excellent
F5	0.68 ± 0.02	0.78 ± 0.07	4.8 ± 0.6	1.05 ± 0.06	26.3 ± 0.07	Excellent
F6	0.73 ± 0.06	0.75 ± 0.03	4.5 ± 0.3	1.02 ± 0.06	27.3 ± 0.05	Excellent

This report describes in the table 3, the flowability of six different powders designated F1 through F6. Using normal procedures, the bulk and tapped densities were measured, with the bulk density ranging from 0.67 to 0.75 g/cm3 and the tapped density ranging from 0.69 to 0.8 g/cm3. With Carr's index ranging from 2.7% to 5% and Hausner's ratio ranging from 1.02 to 1.08, the powders were

determined to have good to exceptional flowability. Angle of repose, which is linked to particle size, shape, and interparticle interactions, varied from 26.3° to 29°, indicating flow ability ranging from acceptable to exceptional. Overall, the powders displayed outstanding flowability; nevertheless, there was considerable variation in the experimental data, indicating that more research is necessary to establish the repeatability of the findings. (table 3)

Table 4: Evaluation Parameters of Praziquantel Chewable Tablet

Parameters	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**
Weight variation	399.3 ± 5	397.6 ± 5	385.8 ± 5	387.6 ± 5	392.8 ± 5	393.7± 5
Hardness	7.6 kg/cm^2	7.5 kg/cm^2	7.4 kg/cm^2	7.4 kg/cm^2	7.2 kg/cm^2	7.1 kg/cm^2
Friability	0.17%	0.21%	0.18%	0.16%	0.19%	0.24%
Disintegration	187 sec	181 sec	152 sec	129sec	159sec	136sec

The table 4 presents data on various quality control parameters of six different formulations (F1 to F6) of a drug. The parameters evaluated include weight variation, hardness, friability, and disintegration time. The data suggests that all formulations meet the pharmacopoeial standards for weight variation and hardness. The disintegration time for formulations F4 and F6 are lower compared to other formulations, indicating faster drug dissolution in these formulations. The friability values are within acceptable limits for all formulations. Overall, the data suggests that the evaluated formulations are of good quality and meet the required standards, indicating their potential for use in drug delivery systems.

The table 5 contains information regarding the percentage of % cumulative drug release (CDR) for six different formulations (F1 to F6) at various time intervals ranging from 5 to 60 minutes. The statistics indicate that the CDR typically rises as medication release duration increases. F4 and F6 formulas have the greatest %CDRs, whereas F2 formulations exhibit the lowest %CDR. In general, the findings imply that drug release rates vary based on formulations and duration, which might be crucial for developing drug delivery systems and optimizing therapeutic doses.

Table 5: Cumulative drug release of Praziquantel chewable tablet

Time (mins)	**%CDR**	**%CDR**	**%CDR**	**%CDR**	**%CDR**	**%CDR**
	F1	**F2**	**F3**	**F4**	**F2**	**F6**
5	4.6664	11.9488	6.0732	8.81	6.4883	18.753
10	10.5412	19.4624	11.9868	16.55	12.4488	31.9318
15	21.09	29.792	20.0088	27.19	20.5933	44.8098
20	26.98	32.1024	32.5416	39.97	33.3606	50.337
25	31.4032	39.9168	39.7656	48.67	42.6062	63.779
30	44.0192	49.0368	46.7796	58.01	52.5343	73.8652
35	48.3056	54.8608	55.734	66.02	58.1217	83.0678
40	57.7904	59.2	65.814	73.38	66.339	87.7866
45	61.8488	60.2752	72.2148	87.69	76.0305	89.8452
50	72.2304	61.1712	78.5736	93.78	83.447	91.9038
55	72.694	62.0672	79.002	95.38	84.0749	92.3926
60	73.1652	62.4	79.422	95.89	84.6209	92.8908

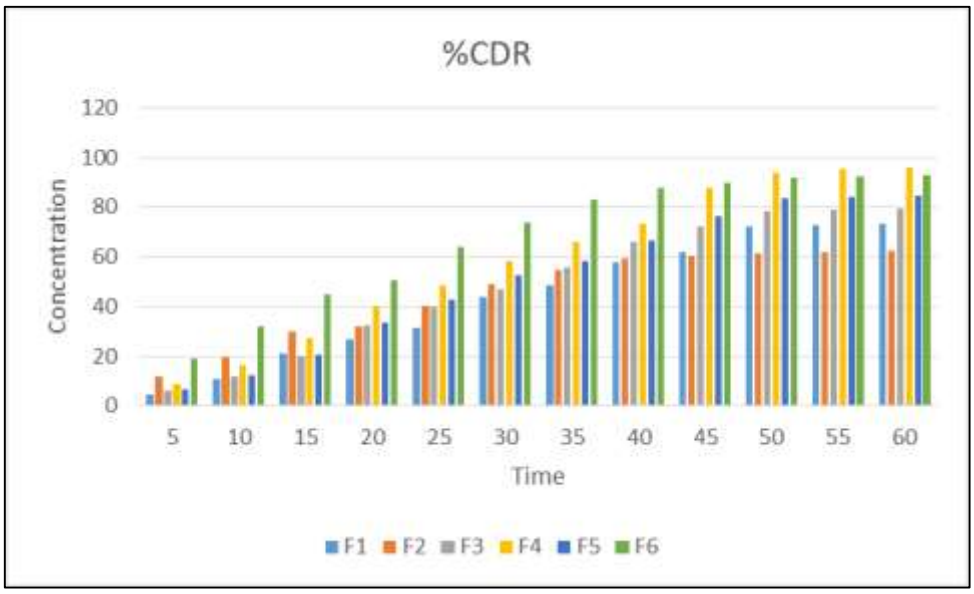

Figure 3: Comparison of % CDR in all six formulations

4. Discussion

The objective of this work was to manufacture chewable tablets of the non-aqueous soluble medication Praziquantel by using variable quantities of binder PVP K30 and super disintegrant in conjunction with the direct compression approach. Infrared spectrum analysis demonstrated that there is no interaction between the medicine and excipients, guaranteeing that the drug content is constant. With the friability test confirming abrasion resistance and the hardness range from 7.1 to 7.6kg/cm2, the dosage quality was constant. Within 5%, there was no variation in the weight of tablets.

In addition, the invitro dissolution profile of chewable tablets was found to increase as the super disintegrant level increased. According to the results of disintegration trials, formulations 4, 5, and 6 disintegrated quickly and efficiently, in accordance with USP criteria. During dissolving trials, formulations 4 and 6, which included less binder and more super disintegrant, exhibited a fast increase in cumulative drug release. Within 60 minutes, these formulations achieved cumulative drug release rates of 95.89% and 92.89 %, fulfilling USP dissolving criteria.

The findings imply that the use of a direct compression approach with changing levels of binder and super disintegrant, which do not interact with the medicine, leads in medication quality that is constant. Increased super-disintegrants and decreased binder give a potential strategy for the formulation of chewable tablets of the non-aqueous-soluble drug Praziquantel with enhanced dissolving rates. This research gives valuable insights for the creation of chewable tablets to treat parasite infections.

5. Conclusion

In conclusion, the development of Praziquantel chewable tablets using a direct compression technique with different quantities of binder and super disintegrants was successful. The absence of any interaction between the drug and excipients was confirmed by infra-red spectral analysis. The medication quality in all tablet batches was consistent, as indicated by the friability test, hardness test, and weight uniformity test. The results of the dissolution studies revealed a rapid and significant drug release in formulations 4 and 6, which contained less binder and higher super disintegrant levels. The in vitro dissolution profile of chewing tablets increased with an increase in super disintegrant levels. Therefore, the use of less binder and higher super disintegrant levels in the tablet formulation containing hydrophilic carriers of the drug is a promising approach to prepare efficient chewing tablets of the non-aqueous soluble drug Praziquantel. These findings could be useful in the development of Praziquantel chewable tablets, which could offer improved patient compliance, particularly in pediatric populations, and ultimately lead to better treatment outcomes.

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