



FORMULATION AND EVALUATION OF TASTE MASKED DISPERSIBLE TABLETS OF CHLOROQUINE PHOSPHATE

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Article Received on: 07/07/12 Revised on: 11/08/12 Approved for publication: 02/09/12

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ABSTRACT

The primary aim of present work was to formulate and evaluate taste masked dispersible tablets of Chloroquine phosphate, an antimalarial drug, using ion exchange resins like INDION 294 and TULSION 339 as a taste masking agent and superdisintegrating agents like crospovidone and sodium starch glycolate in different concentrations. Characterization of drug was done by melting point determination, FT-IR spectroscopy and UV-spectroscopy. Drug-resin complexes were prepared by batch method using the resins in different ratios. Drug loading study was carried at different pH. INDION 294 showed highest drug loading (93.31%). Hence, further studies were done using INDION 294. The drug-resin complexes were studied for micromeritic properties, *in vitro* drug release and taste masking ability by determining threshold bitterness concentration of the drug. The complexes were characterized by drug content, FTIR and DSC studies. Powder blends were prepared and evaluated for various physical properties. Dispersible tablets of drug-resin complex (DRC) were prepared by wet granulation method using crospovidone and sodium starch glycolate in different concentrations as superdisintegrants. Tablets were evaluated for thickness, hardness, friability, uniformity of weight, dispersion time, uniformity of dispersion, disintegration time, wetting time, wetting volume, content of active ingredient and dissolution studies. All the formulations showed the evaluated parameters within the acceptable limits for dispersible tablets. Finally, formulation F3 was taken as an optimized formulation which was containing 3% of crospovidone and showed the least *in vitro* disintegration time and an excellent drug release. Stability study was also conducted on the optimized batch F3 which showed good results.

Key words: Chloroquine phosphate, ion exchange resins, tastes masking, crospovidone, dispersible tablets.

INTRODUCTION

Essential factors in assessing the patient's acceptability of a pharmaceutical product are appearance, odour and taste. Good flavor and texture are found to significantly affect acceptance of the product¹. Oral dosage forms which suffer problems of bitter taste may include chewable tablet, capsule, suspension, lozenges, mouthwashes, dentifrices, syrups and ingestible ointments. Bitter taste is one of the important formulation problems; more than 50% pharmaceutical active ingredients taste bitter. So, for the pediatric and geriatric patient compliance, it's required to mask the taste by suitable technique. Administration of the bitter drug orally with acceptable level of palatability is key issue for health care providers especially in case of pediatric patients.

Over a decade, the demand for development of dispersible tablets has enormously increased as it has significant impact on the patient compliance. Dispersible tablets offer an advantage for populations who have difficulty in swallowing². It has been reported that dysphasia (difficulty in swallowing) is common among all age groups and more specific with pediatric, geriatric population along with institutionalized patients and patients with nausea, vomiting, and motion sickness complications. DTs with good taste and flavor increase the acceptability of bitter drugs by various groups of population³.

Chloroquine phosphate is widely used in the treatment of malaria and it is widely prescribed in pediatric patients. Its bitter taste is a major problem in the pharmaceutical industry due to low patient compliance and remains a huge challenge. So, present work attempts to mask the bitter taste of Chloroquine phosphate.

After extensive literature survey and market study, it was found that Chloroquine phosphate is no where available in DT form. DTs have so many advantages over liquid preparations and conventional tablets available in the market.

So, present work was also aimed at formulating the DT of Chloroquine phosphate.

MATERIALS AND METHOD

Materials

Chloroquine phosphate, the ion exchange resins INDION 294 and TULSION 339 were obtained as a gift sample from Cadila Health Limited, Mumbai, India. Crospovidone and sodium starch glycolate were procured from Signet Chemical Corporation Pvt. Ltd., Mumbai, India. Polyvinyl pyrrolidone K-30 and aspartame were procured from Himedia Lab. Pvt. Ltd., Mumbai, India. Mannitol (spray dried) and magnesium stearate were procured from Sd fine-chem Limited, Mumbai, India and Microcrystalline cellulose was procured from Matrix Lab. India, Nasik, India. All the chemicals and reagents were of analytical reagent grade and distilled water was used through the experiment.

Preformulation Studies

Solubility analysis⁴

In Preformulation studies, solubility analysis was done to select a suitable solvent system to dissolve the drug and also to test its solubility in the dissolution medium which was to be used.

Melting Point determination^{5,6}

Melting point determination of the obtained sample was done which is a good indication of purity of the sample drug since the presence of even small amount of impurity can be detected by lowering or widening in the melting point range.

Organoleptic study⁷

The drug sample was tested for the organoleptic parameters like appearance, colour, odour, and taste and compared with the standard description for Chloroquine phosphate.

FTIR spectroscopic studies⁸

FT-IR absorption spectrum of the drug sample was recorded by KBr dispersion technique over the range of 400 to 4000 cm^{-1} and it was compared with the standard FT-IR spectrum of the pure drug.

Selection of Resins

Resins were selected on the basis of nature of drug and requirements of formulation. Chloroquine phosphate is basic in nature with amine functional groups. Therefore, cation exchange resins were selected. Weak cation exchangers like INDION 294 and TULSION 339 were selected to obtain drug resin complex (DRC) of Chloroquine phosphate.

Compatibility Studies⁹

Fourier Transform Infrared Spectroscopic (FTIR) analysis

FT-IR spectral studies were carried on FT-IR 460 PLUS by JASCO series II instrument using DRIFT method (JASCO Analytical Instruments, Madison, WI) to check the compatibility between drug and excipients. The FT-IR spectrum of drug with excipients was compared with the FT-IR spectrum of the pure drug. Scanning was done from 4000 to 400 cm^{-1} .

Preparation of Taste Masked Product¹⁰

The drug resin complexes were prepared by batch process. An accurately weighed amount of Chloroquine phosphate (500 mg) was dissolved in 100 ml distilled water. Then known weight (500mg) of ion exchange resin was added to the solution and stirred on magnetic stirrer. Time to reach equilibrium was determined by periodically measuring concentration of drug solution. DRC thus formed was filtered and washed with 10 ml of distilled water. The drug content in the final filtrate was analyzed by UV-spectroscopy at 343nm. The amount of drug adsorbed was determined by the difference between amount of drug present in stock solution and amount remaining in filtrate at the end of equilibrium. DRC were dried overnight in a hot air oven at 50°C and then stored in tightly closed in desiccators.

Selection of Drug: Resin Ratio

Four batches were prepared containing drug-resin in the ratio of 1:0.5, 1:1, 1:1.5 and 1:2. The slurry was stirred for 2 hours. DRC obtained were separated by filtration, washed with copious quantity of deionized water and drug contents were determined.

Effect of pH on Drug Loading

A series of 100ml of dispersion containing 1mg/ ml Chloroquine phosphate was prepared. pH of these solutions were adjusted to 2, 3, 4, 5, 6 and 7 using 0.1N HCl; ion exchange resin (100mg) was added to each beaker and stirred for 2 hours. Resinate thus formed was filtered and washed with 10 ml distilled water. The drug content in the final filtrate was analyzed by UV-spectroscopy at 343nm.

DSC analysis of Taste Masked Products

Differential Scanning Calorimetric (DSC) analysis was performed for pure Chloroquine phosphate, INDION 294 and resinate (1:1.5 ratio) using a Mettler Toledo DSC 823e instrument operated with STARE programme under pressure of nitrogen gas with flow rate of 40ml/min and heating rate of 10°C per minute in the temperature range of 30°C to 300°C. Each sample was accurately weighed (3 mg) in an aluminum pan, crimped and hermetically sealed.

Evaluation of Taste Masked Products¹¹

The taste masked products were evaluated for the micromeritic properties like angle of repose, bulk density, tapped density, Carr's index and Hausner's ratio and also for drug content.

Taste Evaluation of the Taste Masked Products^{12, 13}

Evaluation of taste was done in two parts -

Determination of Threshold Bitterness Concentration

Various concentrations (10-50 mcg /ml) of drug were prepared in phosphate buffer pH 6.7. Mouth was rinsed with

buffer solution and then, 10 ml of most dilute solution was tasted by swirling it in the mouth mainly near the base of the tongue for 30 seconds. If the bitter sensation was no longer felt in the mouth after 30 seconds, the solution was spat out and waited for 1 minute to ascertain whether this is due to delayed sensitivity. Then mouth was rinsed with safe drinking water. The next highest concentration should not be tasted until at least 10 minutes had passed. The threshold bitter concentration is the lowest concentration at which a material continues to provoke a bitter sensation after 30 seconds. After the first series of tests, mouth was rinsed thoroughly with safe drinking water until no bitter sensation remained. Interval of at least 10 minutes was observed between two tests.

b) *In Vitro* Evaluation of Taste of Resinates

An accurately weighed (equivalent to 100 mg drug) taste masked product and 10 ml of pH 6.7 phosphate buffer (0.1 M) was taken in series of volumetric flask and stirred at 50 rpm. The stirring was stopped at different time intervals such as 0, 10, 30, 60 and 120 sec., dispersion was filtered, and the concentration of chloroquine phosphate in filtered resinate was determined. Time for resinate to achieve drug concentration corresponding to threshold bitterness in 10 ml phosphate buffer was recorded.

In Vitro Drug Release Profile

The *in vitro* dissolution study of Chloroquine phosphate taste masked products was carried using 0.1N HCL as a dissolution medium in Type II USP dissolution apparatus at 37°C $\pm$ 0.5°C for 60 minutes. At 10 min. interval aliquots of medium (5 ml) were taken, filtered and absorbance was measured by UV spectroscopy at 343nm. The medium was replaced with equal volume of fresh dissolution fluid after each sampling.

Formulation of Dispersible Tablet of Taste Masked Chloroquine phosphate

Compositions of seven different formulations of Chloroquine phosphate tablets were prepared as given in table 1. Different concentrations of the superdisintegrants, i.e. Croscopolvidone and Sodium starch glycolate were used. Batch F₁ was kept without any superdisintegrants. All ingredients were passed through sieve no. 120, and then weighed accurately and mixed thoroughly (except magnesium stearate). Tablets were prepared by wet granulation method. Granules were prepared by passing the wet mass through sieve no 40. Prepared granules were dried in hot air oven at 45° C. Dried granules were sized through sieve no. 40 placed over sieve no. 60, lubricated with magnesium stearate. All the seven blends were evaluated for various parameters like angle of repose, bulk density, tapped density, % compressibility and Hausner ratio, drug content etc.

Evaluation of Chloroquine phosphate Dispersible Tablets

The tablets from all the batches were evaluated for different parameters as follows:

Appearance⁷

Tablets were evaluated for organoleptic properties.

Thickness¹⁴

Thickness of tablets was determined using Vernier caliper, three tablets from each batch were used and an average value was calculated.

Weight Variation^{7, 14, 15}

Twenty tablets were selected and average weight was determined. Then individual tablets were weighed and the individual weight was compared with an average weight.

Hardness^{7, 14, 15}

Tablets were selected at random from each formulation and hardness was checked using Monsanto Hardness Tester.

Friability^{7, 15}

Pre-weighed sample of tablets was placed in the Roche Friabilator tester, which was then operated for 100 revolutions. Tablets were dedusted and reweighed; tablets should not lose more than 1% of their initial weight.

Content of Active Ingredient^{5, 7}

Drug content of all the batches was determined. For this purpose six tablets were weighed and crushed with pestle in a small glass mortar. The fine powder was weighed to get 1003 mg (equivalent to 250 mg of Chloroquine phosphate) and was placed in 1M HCl (250ml) and stirred at 100 rpm for one hour. The solution was filtered and analyzed for content of Chloroquine phosphate by UV spectrophotometer.

Uniformity of Dispersion^{5, 7}

Two tablets were placed in 100 ml of water and stirred gently until completely dispersed. A smooth dispersion was obtained which passes through a sieve screen with a nominal mesh aperture of 710 μ m (sieve number 22).

Wetting Volume¹⁶

The tablet was placed in the center of the Petri dish and with the help of 5 ml pipette; distilled water was added drop wise on the tablet. The volume required to completely disintegrate the tablet was noted as the wetting volume.

Wetting Time^{14, 17}

A piece of tissue paper (12cmx10.75cm) folded twice was placed in a Petri dish (10 cm diameter) containing 10 ml of

water. Containing Eosin, a water soluble dye, was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper and allowed to wet completely. The time required for water to reach upper surface of the tablet was noted as a wetting time.

Dispersion Time^{14, 17}

Tablet was added to 10 ml of water and time required for complete dispersion was measured. Three tablets from each formulation were randomly selected and dispersion time was performed.

Disintegration Time¹⁸

The disintegration time of tablet was measured in water (37°C) according to U.S.P. disintegration test apparatus. Three trials for each batch were performed.

In vitro Dissolution⁴

The in vitro dissolution study was performed in the U.S.P. apparatus type II. Aliquot equal to 5 ml of dissolution medium was withdrawn at specific interval and replaced with fresh medium for maintaining sink condition. Sample was filtered and absorbance of filtered solutions determined by UV spectroscopy at 343 nm. Dissolution rate was studied for all formulations.

Accelerated Stability Study¹⁹

Accelerated stability studies were carried out on optimized formulation F3 for one month period as prescribed by ICH guidelines for accelerated study at 40 $\pm$ 2°C and RH 75 $\pm$ 5 %. The tablets were analyzed for physical characterization, dissolution and drug content and compared with the same before accelerated stability study.

Table No. 1: Composition of taste masked dispersible tablets of Chloroquine phosphate with corresponding formulations

Sr. No	Formulations Ingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)
1.	DRC	628	628	628	628	628	628	628
2.	PVP K-30	83	85	86	87	85	86	87
3.	Mannitol	183	179	177	175	179	177	175
4.	Magnesium stearate	3.5	3.5	3.5	3.5	3.5	3.5	3.5
5.	Crospovidone	-	17(2%)	26(3%)	34(4%)	-	-	-
6.	Sodium Starch glycolate	-	-	-	-	17(2%)	26(3%)	34(4%)
7.	Aspartame	20	20	20	20	20	20	20
8.	MCC	83	85	86	87	85	86	87
9.	Flavour	2.5	2.5	2.5	2.5	2.5	2.5	2.5
	Weight/Tablet	1003	1003	1003	1003	1003	1003	1003

Table No. 2: Micromeritic properties of tablet blends

Formulation Code	Angle of Repose* (θ°)	Bulk Density* (g/cm ³)	Tapped Density* (g/cm ³)	Compressibility Index*	Hausner's Ratio*
Pure drug	35.20 $\pm$ 0.56	0.526 $\pm$ 0.03	0.636 $\pm$ 0.02	17.30 $\pm$ 0.58	1.20 $\pm$ 0.009
DRC	26.57 $\pm$ 0.87	0.449 $\pm$ 0.02	0.498 $\pm$ 0.02	9.83 $\pm$ 0.38	1.11 $\pm$ 0.009
F1	25.70 $\pm$ 1.31	0.456 $\pm$ 0.01	0.523 $\pm$ 0.01	12.81 $\pm$ 0.30	1.15 $\pm$ 0.003
F2	27.25 $\pm$ 1.81	0.480 $\pm$ 0.01	0.546 $\pm$ 0.01	12.09 $\pm$ 0.33	1.14 $\pm$ 0.004
F3	26.51 $\pm$ 1.17	0.429 $\pm$ 0.02	0.490 $\pm$ 0.01	12.45 $\pm$ 1.81	1.14 $\pm$ 0.02
F4	26.77 $\pm$ 0.73	0.461 $\pm$ 0.01	0.522 $\pm$ 0.01	11.69 $\pm$ 0.30	1.13 $\pm$ 0.003
F5	26.42 $\pm$ 1.15	0.447 $\pm$ 0.03	0.512 $\pm$ 0.02	12.70 $\pm$ 1.51	1.15 $\pm$ 0.02
F6	26.22 $\pm$ 1.25	0.468 $\pm$ 0.02	0.541 $\pm$ 0.02	13.49 $\pm$ 1.51	1.16 $\pm$ 0.02
F7	26.34 $\pm$ 1.13	0.469 $\pm$ 0.02	0.544 $\pm$ 0.01	13.79 $\pm$ 1.51	1.16 $\pm$ 0.02

*Average of three determinations
 $\pm$ Standard deviation

Table No. 3: Physical evaluation of tablet formulations

Formulation Code	Weight Variation* (g)	Hardness* (kg/cm ²)	%Friability*	Thickness* (mm)
F1	1.003 $\pm$ 0.030	3.60 $\pm$ 0.16	0.262 $\pm$ 0.01	3.43 $\pm$ 0.09
F2	1.005 $\pm$ 0.036	3.53 $\pm$ 0.09	0.359 $\pm$ 0.10	3.46 $\pm$ 0.04
F3	1.005 $\pm$ 0.032	3.78 $\pm$ 0.09	0.286 $\pm$ 0.02	3.43 $\pm$ 0.09
F4	1.008 $\pm$ 0.039	3.60 $\pm$ 0.16	0.389 $\pm$ 0.03	3.44 $\pm$ 0.09
F5	1.005 $\pm$ 0.041	3.85 $\pm$ 0.16	0.390 $\pm$ 0.03	3.42 $\pm$ 0.08
F6	1.004 $\pm$ 0.043	3.85 $\pm$ 0.16	0.394 $\pm$ 0.01	3.48 $\pm$ 0.08
F7	1.003 $\pm$ 0.039	3.82 $\pm$ 0.16	0.392 $\pm$ 0.03	3.48 $\pm$ 0.08

*Averages of three determination

$\pm$ Standard deviation

Table No. 4: Evaluation of tablet formulations

Formulation Code	Wetting Time* (sec)	Wetting Volume* (ml)	Uniformity of Dispersion*	Content of Active Ingredients (%)
F1	72 ± 4	6.4 ± 0.2	Passes	96.86
F2	46 ± 2	4.8 ± 0.1	Passes	98.56
F3	29 ± 1	4.2 ± 0.2	Passes	98.76
F4	25 ± 2	4.4 ± 0.2	Passes	96.91
F5	42 ± 2	4.5 ± 0.2	Passes	97.94
F6	35 ± 2	4.3 ± 0.1	Passes	98.70
F7	31 ± 2	4.4 ± 0.2	Passes	98.76

*Averages of three determination

± Standard deviation

Table No. 5: *In vitro* drug release study of seven formulations

Time (min)	F1 (%)*	F2 (%)*	F3 (%)*	F4 (%)*	F5 (%)*	F6 (%)*	F7 (%)*
10	39.55 ± 1.11	42.28 ± 2.23	47.75 ± 1.38	52.31 ± 1.49	40.46 ± 2.11	40.46 ± 1.15	42.28 ± 1.43
20	47.75 ± 2.2	52.31 ± 1.25	71.45 ± 1.42	77.83 ± 0.48	49.57 ± 2.34	60.51 ± 1.58	53.22 ± 1.57
30	57.78 ± 1.6	61.42 ± 1.49	97.88 ± 0.33	98.79 ± 0.21	59.60 ± 1.51	62.33 ± 1.72	64.16 ± 1.44
40	69.63 ± 2.10	79.65 ± 1.62	98.79 ± 0.10	98.81 ± 0.19	72.36 ± 1.64	75.09 ± 0.78	77.83 ± 2.05
50	84.21 ± 2.15	97.88 ± 0.18	98.80 ± 0.12	98.80 ± 0.19	80.56 ± 1.21	96.06 ± 0.25	96.03 ± 0.78
60	96.05 ± 0.15	97.88 ± 0.15	98.42 ± 0.22	98.79 ± 0.15	96.06 ± 0.41	96.09 ± 0.24	98.79 ± 0.41
70	96.06 ± 0.13	97.79 ± 0.18	98.45 ± 0.23	98.80 ± 0.20	96.08 ± 0.44	96.08 ± 0.21	98.80 ± 0.39

*Averages of three determination

± Standard deviation

Table No. 6: Evaluation of optimized batch F3 after stability study

Formulation Code	Thickness (mm)	Hardness (kg/cm ²)	Friability (%)	Percent drug content
F3	3.43 ± 0.09	3.76 ± 0.09	0.283	98.69

RESULTS AND DISCUSSION

Preformulation study revealed that Chloroquine phosphate sample was found to be freely soluble in water and slightly soluble in ethanol (90%), methanol, ether and chloroform. The melting point of the obtained drug sample was found to be 212°C, which is within the given standard range 210-215°C. The physical state, colour, odour and taste of the drug sample were found to be crystalline, white, odourless and bitter respectively, indicating its compliance with IP standards. The FTIR spectrum of the drug sample was found to be similar to the standard spectrum of Chloroquine phosphate. It was observed that all the characteristic peaks of Chloroquine phosphate were present in the sample drug spectrum, indicating purity of the sample.

The study of drug-resin complexes prepared using INDION 294 and TULSION 339 showed that Chloroquine phosphate: INDION 294 (1: 1.5) gave the best drug loading as 97.57 % and the drug content of resinate was 39.82% and INDION 294 also gave better loading efficiency i.e. $93.31 \pm 1.12\%$ at 2 hrs. Hence, it was selected for the further studies.

It was observed that with increasing pH up to 6, the loading of drug on resin increased but above pH 6 loading decreased. Since the drug has pKa of 8.1 and 9.94 it will be ionized throughout most of the GIT but the resin being a weak carboxylic acid will be better ionized above a pH of 5 hence the drug loading improves beyond this pH.

Compatibility Study

From the FT-IR spectra of the pure drug and the spectrum of the physical mixture (drug with the +excipients), it was observed that all the characteristic peaks of Chloroquine phosphate, i.e. peaks for N-H stretch, C-N ring stretch, C=C stretch and C-Cl stretch were present in the pure drug as well as in combination spectrum. Thus, it indicated that all the excipients were compatible with Chloroquine phosphate.

Differential Scanning Calorimetric Study

DSC thermogram of pure Chloroquine phosphate showed an endotherm at 246.75°C corresponding to melting while DSC thermogram of INDION 294 resin did not show any sharp peak but showed only a slight curve in the range around 102.57-167.51°C. The DSC thermogram of Chloroquine

phosphate: INDION 294 complex also did not show any sharp peak; rather it showed a very broad endotherm in the range 191.06-226.24°C. Also, sharp endotherm due to melting of Chloroquine phosphate was disappeared which supports the conclusion that complexation between Chloroquine phosphate and INDION 294 has occurred. All this is illustrated in Fig.1.

The micromeritic study revealed that the flow and compressibility of the drug-resin complexes were within acceptable range.

The threshold bitterness for the pure drug was to be found at 40 µg/ ml. After the DRC was added to simulated salivary fluid (phosphate buffer pH 6.8), even after 2 minutes the threshold bitterness concentration was not achieved. This shows the bitterness masking ability of the DRC.

The *in vitro* drug release study of the DRC showed near about 100 % cumulative drug release within 60 min. This could be due to the rapid exchange of drug with counter ions present in the dissolution medium till equilibrium was established. It is shown in the Fig. 2.

The outcomes of study of the micromeritic properties of the prepared granules indicated good flow properties and moderate compressibility of the granules. It is shown in Table No. 2.

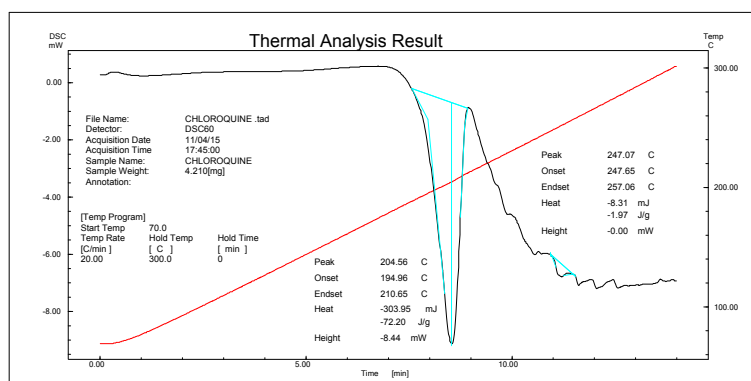
All the formulated dispersible tablets showed thickness in the range of 3.42 - 3.48mm, weight range in 1.003 – 1.008g, hardness in the range of 3.50 – 3.85kg/cm² and friability in the range of 0.252 - 0.394%. Thus all the physical parameters of all formulations were within IP limits. This is given in Table No. 3.

Drug content of all the batches was in the range of 96.86%-98.76% which is within the I.P. limit. All the batches pass the Uniformity of dispersion as per Indian Pharmacopoeia. The wetting time and wetting volume of all the batches were found to be within the range of 25-46 sec., and 4.2-4.8ml, respectively except of batch F1 for which those were 72 sec. and 6.4ml, respectively. This indicated rapid absorption of water by the tablets.

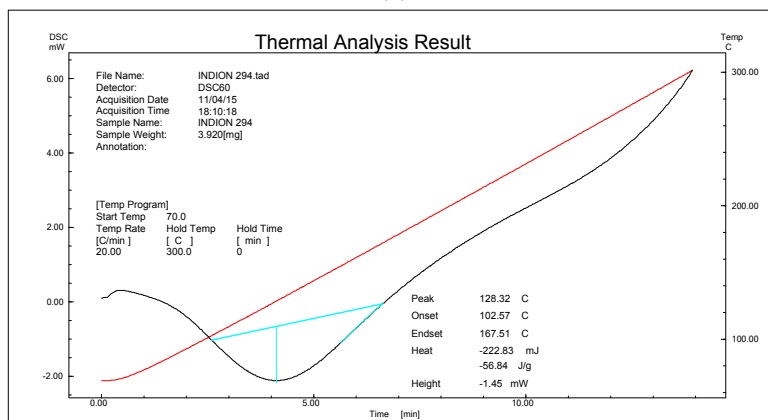
The dispersion time of all the batches tablet was within the range of 41-56 sec., except F1 which is 85 sec. Formulations

F3 and F4 demonstrated least dispersion time of 42 sec. and 41 sec. respectively. In these formulations, Crospovidone was used in 3% and 4% concentration respectively. The disintegration time of all the batches was within the range of 31-49 sec, except F1 which is 72 sec. Formulations F3 and F4 demonstrated a complete disintegration time of 31 sec. The *in vitro* drug release study showed that the percentage drug release of all the batches was found to be within 96.06 to 98.80% in 70 min. This was within the acceptable limits. It is shown in Table No. 5 and illustrated in Fig. 3. Formulation F3 (Crospovidone 3%) showed disintegration time of 31 sec., dispersion time of 42 sec. and more than 98%

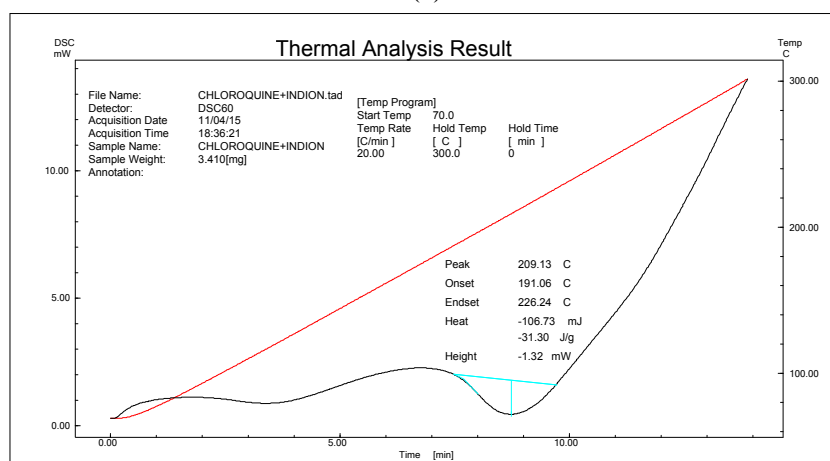
in vitro drug release within 40 min. which was quite better than other formulations and equivalent to formulation F4 (Crospovidone 4%). Hence formulation F3 was considered as an optimized formulation and subjected for stability study. In the stability study carried out on the formulation F3, it was found that there were no substantial changes in all parameters. The results revealed that product was sufficiently stable for the period of 30 days at $40^{\circ}\text{C} \pm 2^{\circ}\text{C} / 75 \pm 5 \% \text{ RH}$. Dissolution profile of optimized batch F3 before and after stability revealed that no significant changes occurred during stability study period. Thus, it can be concluded that tablets (formulation F3) were stable. It is shown in Fig. 4.



(A)



(B)



(C)

Fig.1: DSC thermograms of pure Chloroquine phosphate (A), resin INDION 294 (B) and Chloroquine phosphate: INDION 294 resin (1:1.5 ratio) (C)

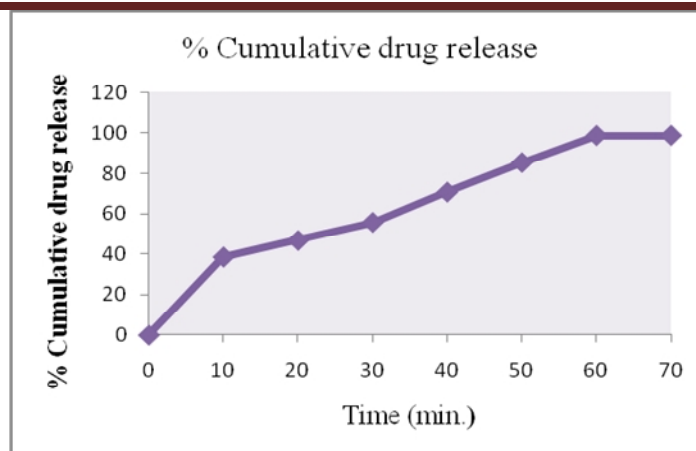


Fig. 2: Cumulative % release of Chloroquine phosphate from DRC

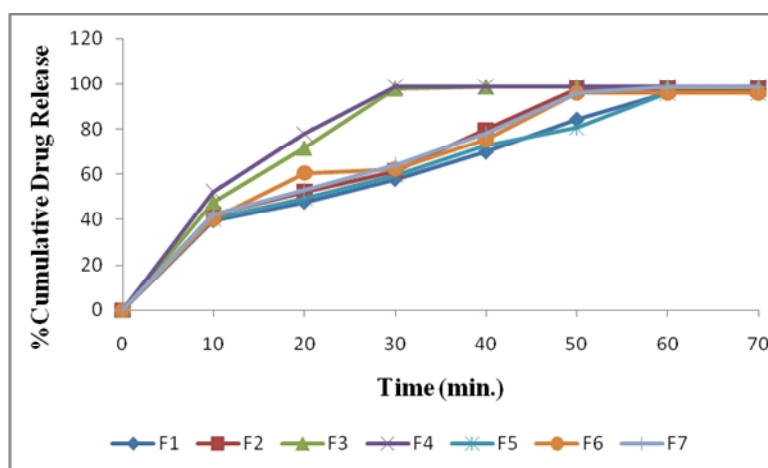


Fig. 3: In vitro drug release profile of seven formulations

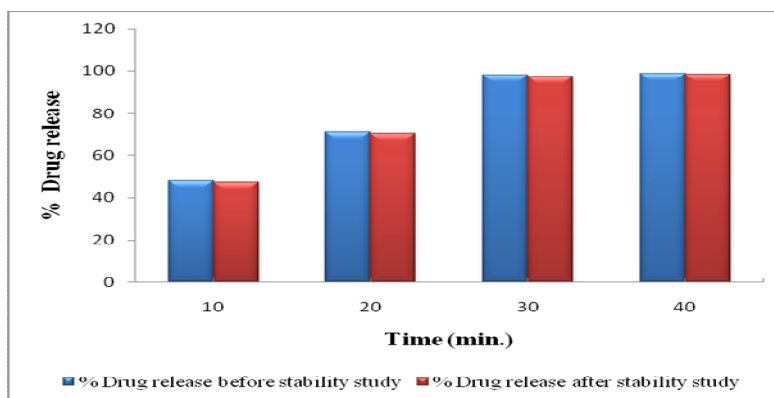


Fig. 4: Comparison of drug release study of batch F3 before and after stability study

CONCLUSION

Overall, the results suggested that ion exchange resins form a suitable tool to mask the bitter taste of drug like Chloroquine and improve pediatric patient compliance. Also, the results indicated that taste masked dispersible tablets of Chloroquine phosphate can be formulated successfully by using INDION 294 and crospovidone as a taste masking and superdisintegrating agent, respectively. And this approach may be an alternative for the conventional method. It was also concluded that technique of addition of superdisintegrants is a useful method for preparing dispersible tablets by wet granulation method. The present study demonstrated potentials for rapid absorption, improved bioavailability, effective therapy and patient compliance.

ACKNOWLEDGEMENT

The authors greatly acknowledged the Cadila Health Limited, Mumbai, India, for the gift samples of Chloroquine

phosphate, INDION 294 and TULSION 339. The authors are grateful to the School of Pharmacy, Swami Ramanand Teerth Marathwada University, Nanded, MS, India for providing all the necessary facilities for carrying out the experimental studies.

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Source of support: Nil, Conflict of interest: None Declared