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PROCESS VALIDATION OF COATED LARIAGO TABLET

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Abstract: Chloroquine was used as a prophylactic agent against malaria, and more recently as a mild immunosuppressive. However, due to lengthy treatment periods, adverse effects have become apparent, which included retinopathy. The structurally related hydroxychloroquine is less toxic, thought to be owing to a lower tissue accumulation in melanin rich areas. This study primarily focused on quantifying melanin binding between chloroquine and hydroxychloroquine at physiological pH to investigate the potential link between binding and reported toxicity. In addition, for the first time this study quantified the actual extent of adsorption of chloroquine and hydroxychloroquine to melanin and examined the desorption profile of both drugs from melanin to demonstrate the affinity between the pigment and the solutes. The results suggest that there is a difference between the adsorption affinities of chloroquine and hydroxychloroquine, potentially explaining the differences in bioaccumulation in retinal tissue. In addition, both solutes displayed a strong physical attraction to the absorbent.

I. INTRODUCTION

In an environment of increasing global cutting edge competition where countries with lower production cost quickly catch up technologically, a new thinking is required in ordered to meet the competition. A proactive way to meet the increasing competition is to focus on maximizing the utilization of existing technology and faster than the competitions, being able to continuously introduces and make use of new technology. In this endeavor sourcing of the product to third party or own location is gaining world wide acceptance. Once the manufacturing site is approved next step entail the regulatory submission for marketing authorization. In support of which process validation data play an important role.

The supportive data should show the pharmaceutical equivalence between the product manufactured at the donor and the recipient site. The data should show that the process is under control with no significant variation in the critical parameter. A successful industrial validation thus entails the validation approach encompassing the whole chain. A manufacturer may decide to validate the process to improve the over all quality, eliminate scrap, reduce cost, and to improve the customer satisfaction, or other reasons.

Validation is a concept that has been evolving continuously since its first formal appearance in the United States in 1978. The concept of validation has expanded through the years to encompass a wide range of activities from analytical methods used for quality control of drug substances and drug products to computerized systems for clinical trials, labeling or process control, validation is based on regulatory requirements, and is an important and integral part of Current Good Manufacturing Practices.Validation is one element of quality assurance associated with particular processes, as the process differs so widely, there is no universal approach to validation and regulatory bodies such as Food & Drug Administration and European Committee have developed general non mandatory guidelines.

Validation is a relatively new concept in pharmaceutical manufacturing to ensure total quality management and to assure product of best quality. Currently, validation concept are being recognized for their value in helping to assure the quality features of classes of drug products other than sterile products also.

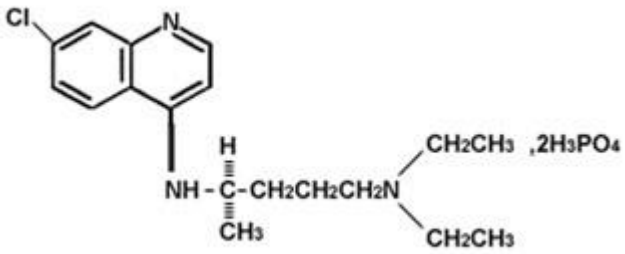
II.RESEARCH ENVISAGED

Validation is needed to maintain quality, consistency, and safety. Validation is a rapidly growing and evolving subject. The machine automation and process control in the pharmaceutical industry has caused additional concerns relating the validation of the processing system. Validation is responsible for providing higher degree of assurance for the product.

Validation generally requires meticulous preparation and careful planning of the various steps in the process. In addition, a work should be carried out in a structure way according to formally authorized standard operating procedure. All observation must be documented and where ever possible must be recorded as actual numerical results.

IIII. DRUG PROFILE

CHLOROQUINE PHOSPHATE



Molecular formula		Mol. Wt
$C_{18}H_{26}ClN_3,2H_3PO_4$	.	515.87

IUPAC NAME:-

Chloroquine Phosphate is *(RS)*-4-(7-chloro-4-quinolyl- amino)pentyldiethylamine diphosphate.

Category: Antimalarial; antiamoebic.

Dose: Chloroquine. Prophylactic, 300 mg once weekly; therapeutic, initial dose, 600 mg followed by a single dose of 300 mg after 6 to 8 hours and then by a single dose of 300 mg daily for the next 2 to 4 days; by slow intravenous infusion, 200 to 300 mg (antimalarial); by intramuscular injection, 160 to 200 mg repeated at intervals of 12 hours until oral therapy is possible (antimalarial and in hepatic amoebiasis) 600 mg daily for 5 to 7 days followed by 300 to 450 mg daily or twice a week for 2 weeks or longer; by intramuscular injection, same dose as for malaria therapy (in hepatic amoebiasis 250 mg of chloroquine phosphate is approximately equivalent to 155 mg of chloroquine).

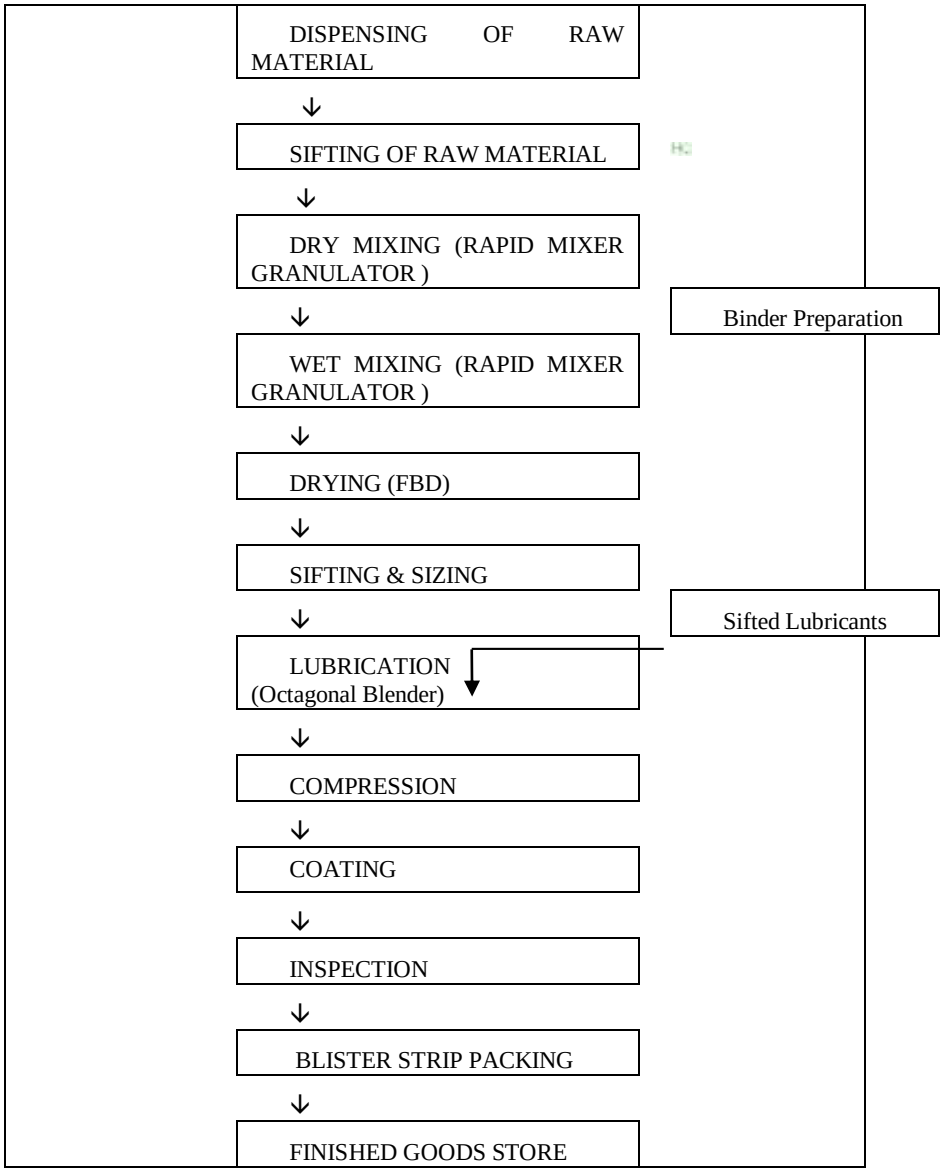
pH: Between 3.5 and 4.5, determined in a 10.0% w/v solution.

Clarity of solution: A 10.0% w/v solution in *carbon dioxide-free water* is *clear*.

Heavy metals: Not more than 10 ppm, determined on 2.0 g by Method A.

Related substances: Carry out the method for *thin-layer chromatography*, using *silica gel GF254* as the coating substance and a mixture of 50 volumes of *chloroform*, 40 volumes of *cyclohexane* and 10 volumes of *diethylamine* as the mobile phase but allowing the solvent front to ascend 12 cm above the line of application.

IV. PLAN OF WORK



V.

EXPERIMENTAL WORK

S. No.	Process stage	Variables	Justification	Sampling	Acceptance Criteria
1	Dry Mixing	• Speed of RMG • Time	Homogenous mixing of all materials	Each 2 gm sample from 5 different locations Top Right, Top Left, Middle & Bottom Left., Bottom Right & one composite sample from each layer top layer, Middle layer & Bottom Layer From RMG After 5 min. mixing. (Total 8 sample)	Assay : Chloroquine Phosphate IP 250 mg /Tab. 97.0% –103.0%
2	Binding	• Speed of mixer • Binder Quantity • Binding Time	Uniform dough mass to form	Physical verification	Uniform dough mass should be formed
3	Drying	• Temperature • Time	Uniformly dry the Granules	5 sample taken Top Right, Top Left, Middle, Bottom Right & Bottom Left from FBD Bowl	LOD of Granules between 3.5 – 5.0% w/w.
4	Lubrication	• Speed of blender • Time	Distribution of lubricants in homogenous mixing with dry Granules	Un lubricated granules mixed for 5 min & collect One Composite sample for LOD of Granules	LOD of Granules between 3.5 – 5.0% w/w.
				Each 2 gm sample from 9 different locations Top Right, Top center, Top Left, Middle Left, Middle center, Middle Right, Bottom Left., Bottom center & Bottom Right (Total 9 sample) From Octagonal Blender After 25 min. mixing.	Assay : Chloroquine Phosphate IP 250 mg /Tab. 97.0% –103.0%
				One Composite sample after addition with magnesium stereate after 5 min. mixing collect	Bulk density, sieve Analysis & Loss on Drying 3.5 – 5.0% w/w
5	Compresion	• Hopper Level • Speed of Machine	All compressed core tablet comply with specification of core tablets	Sampling: Initial, middle, End of compression at selected speed 30 ± 5 RPM	
				Acceptance Criteria: Appearance	White to almost white, circular, biconvex, uncoated tablets.

S. No.	Process stage	Variables	Justification	Sampling	Acceptance Criteria
				Average weight	300 mg ± 2.0% (294 – 306 mg)
				Weight of 20 Tablet	6.00 ± 2.0% (5.880 – 6.120 gm)
				Uniformity of weight	± 5.0 % of Average weight.
				Diameter	9.5 – 9.7 mm
				Thickness	3.8 to 4.4 mm
				Hardness	2.5 – 7.0 Kg/cm^2
				Friability	NMT 1.0 % w/w
				Disintegration test	NMT 15 min.
				Assay	Chloroquine phosphate IP 250 mg/Tab. 97.0% –103.0%
7	Coating	• Pan speed • Inlet Temperature • Exhaust Temperature • Bed Temperature • Air pressure • Spray Rate	To get uniform coating on tablet.	After Coating sample to be collect for In-process checks.	All Coated tablet should comply with specification of Coated tablet. Coated tablet % of weight gain should comply within limit.
8	Blister Packing	• Speed • Temperature	To get proper sealing cutting, Intactness, over coding details and physical appearance	At selected temperature and speed.	-Strip should have aesthetically good appearance, proper sealing, cutting, Intactness and legible batch details over coding - Leak Test : No one tablet should wet and all tablets physical appearance should match with description. Tablets should not stick with foil.

VI. RESULTS AND DISCUSSION

BATCH UNDER VALIDATION

S.No.	Batch No.	Batch Size	Mfg. Date	Started On	Completed On
1.	X	32.0 Lac	March 2012	26.03.12	28.05.12
2.	Y	32.0 Lac	March 2012	28.03.12	15.06.12
3.	Z	32.0 Lac	March 2012	30.03.12	30.06.12

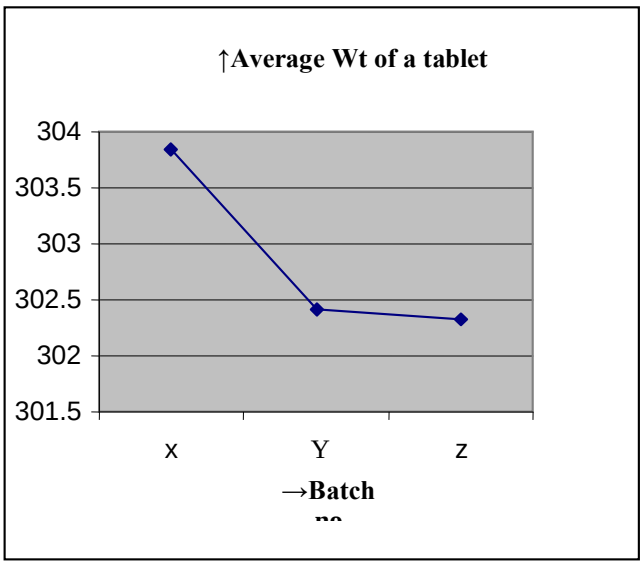
S. No	Name of the Equipment	Qualified (Yes / No)
1.	Sifter	Yes
2.	Air swept sifter with powder transfer system	Yes
3.	Steam Kettle	Yes
4.	Rapid Mixer Granulator	Yes
5.	Multi mill	Yes
6.	Fluid Bed Dryer	Yes
7.	Oscillating Granulator	Yes
8.	Conical mill with powder transfer system	Yes
9.	Octagonal Blender	Yes
10.	Compression Machine	Yes

11.	Coating pan	Yes
12.	Blister Packing Machine	Yes

S. No.	**Process stage**	**Observation**
1.0	**Dry mixing**	Dry mixing performed in Rapid Mixer Granulator for 05 min.
2.0	**Wet mixing and Binding**	Wet mixing performed for 6 - 8 min. at slow speed with slow chopper for 2 – 3 minute and binding at fast speed for 5 - 7 minute & run the chopper at fast speed for 3 – 5 minute. Wet milling done through Co-mill using 15.0mm SS Screen.
3.0	**Drying**	Drying performed in fluid bed dryer. Initial drying at ambient Temperature for 15 min. Final drying at 50 - 60º C Temperature for 25 – 40 min.

Acceptance criteria:

Average Wt of a tablet: 309.0 mg ±5% (293.55 - 324.45mg)



VII. Acknowledgment

In order to excel, you must be completely dedicated to your chosen field. You must also be prepared to work hard and be willing to accept new changes and developments. Without 100% dedication, you won't be able to do this."This report has been kept on track and been seen through to completion with the support and encouragement of numerous people including my well-wishers, my friends, colleagues. I would like to thank all those people who made this report possible and an unforgettable experience for me. I express my thanks to all those who contributed in many ways to the success of this study and made it an unforgettable experience for me.

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References

[1] Prof. Manohar A. Potdar "Pharmaceutical Quality Assurance", Nirali prakashan, second edition dec-2007, p.no. 8.1-8.108
[2] ANNEX 15, EC guide to GOOD MANUFACTURING PRACTICES, Qualification and validation, sept, 2001
[3] Good Manufacturing Practices for Pharmaceutical Products. WHO Expert Committee on Specifications for Pharmaceutical Preparations.32nd Report, WHO Technical Report Series no.823. Geneva: WHO, 1992: pp 14-96.