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Comparative Analysis of Three Brands of Artemether with Lumefantrine Tablets (Pharmaceutics)

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ABSTRACT
Purpose: The aim of the present study is to investigate the physicochemical equivalence of eight brands of tablets containing**Artemether with Lumefantrine Tablets**(antimalarial drug combination) sourced from different retail Pharmacy outlets in the Other countries market.
Method: The quality and physicochemical equivalence of eight different brands of **Artemether with Lumefantrine Tablets**combination tablets were assessed. The assessment included theevaluation of uniformity of weight, friability,Thickness, crushing strength, disintegration as well as chemical assay of the tablets.
Results: All the brands of the tablets passed the Indian Pharmacopoeia (IP) standards for uniformity of weight, disintegration and crushing strength. Three of the eight brands . the friability testthe amounts of **Artemether with Lumefantrine Tablets** released from the different brands ($P>0.05$).
Conclusion: Only three brands (Not registered by NAFDAC) out of the eight brands of **Artemether with Lumefantrine Tablets**that were analysed passed all the BP quality specificationsand were physically and chemically equivalent. This study highlights the need for constantmarket monitoring of new products to ascertain their equivalency to the innovator product.
Keywords: Chemical equivalence, comparative study, Artemether with Lumefantrine Tablets.

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Thank you all for being an integral part of this journey."
(Dr. Mohsin Hasan &VanitaLokhande).

I. INTRODUCTION

Malaria has a long history in India, dating back thousands of years. The disease has been documented in ancient Indian texts, including the Atharva Veda, which dates back to around 1000 BCE. In these texts, malaria is described as "VishamaJwara," meaning intermittent fever.

Throughout history, malaria has been a significant public health challenge in India, particularly in regions with tropical climates that are conducive to the breeding of mosquitoes, which transmit the disease.

During the British colonial period, malaria became a major concern due to the construction of railways, irrigation projects, and other infrastructure developments that created breeding grounds for mosquitoes. The disease had a significant impact on British troops and colonial administrators, leading to efforts to control malaria through measures such as draining swamps and using quinine as a treatment.

After India gained independence in 1947, the government continued efforts to control malaria. The National Malaria Control Programme was launched in 1953, followed by the Malaria

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Eradication Programme in 1958. These efforts focused on the use of insecticides, mosquito nets, and antimalarial drugs to control malaria transmission.

Despite these efforts, malaria remained endemic in many parts of India, particularly in rural and remote areas. In recent decades, there has been a renewed focus on malaria control and elimination, with the introduction of new strategies such as insecticide-treated bed nets, indoor residual spraying, and the use of artemisinin-based combination therapies (ACTs) for treatment.

The government of India has set ambitious goals for malaria elimination, aiming to achieve zero indigenous cases of malaria by 2030. Efforts to achieve this goal include strengthening surveillance, improving access to diagnostics and treatment, and increasing community engagement in malaria control activities.

Methodology

Materials:-

Three brands of **Artemether with Lumefantrine Tablets** (A to C) were obtained from different retail outlets in Other countries. The manufacture and expiry dates are shown in Table 1.

Brand name:-Brand A:- FM Plus.
Brand B:-Lumerax – 80.
Brand C:-Rezatrin Forte.

Table 1: Country of origin, manufacture and expiry dates ofThree brands of **Artemether with Lumefantrine Tablets.**

Brand	Date of Manufacture	Expiry Date	Country of Origin	NAFDAC* Registration
A	Feb, 2023	Jan, 2025	India	No
B	Jul, 2023	May, 2025	India	No
C	Sep, 2023	Aug, 2025	India	No

➢ Weight uniformitiy (WU):-

Ten tablets were selected randomly from each formulation andweighed individually. The individual weights were compared to the mean weight and the standard deviation (SD) was calculated.

IP Standard for tablets for tablets Dosage form :-

SR NO.	Average weight of tablet (Mg)	Maximum % difference allowed
1	80 or Less	10%
2	80 – 250	7.5%
3	More than 250	5%

Calculation :-
X = Number of weight tablets / Number of tablets

➢ Hardness test (HT):-

The hardness of Five or ten tablets from each formulation was testedusing Monsanto hardness tester (Creve Coeur, MO) and the meanand SD values were calculated.
The hardness of the tablets is often measured using a hardness tester.

The formula for tablet hardness is :-

Force applied (N)
Tablet area (cm2)

➢ Thickness variation (TV):-

Ten tablets from each formulation were taken randomly and theirthickness was measured using micrometer (Starrett, Athol, MA,India), and then, the mean thickness and SD were calculated.
The thickness of tablets is a crucial parameters in pharmaceutical manufacturing.

The formula tablets thickness is:-

Tablet weight
Diameter × Bulk Density

Tablet weight is usually specified by the formulation, and tablets Bulk density can be calculated using the tablet diameter and thickness. The surface area formula depends on the shape of tablet (eg. Circular, oval), but for a simple circular tablets its .
Bulk Density = Mass of Tablet / Volume of tablet
Volume of tablet = $\pi \times (D / 2)^2 \times H$

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After obtaining the tablet surface area, you can use it in the thickness formula to calculate the desired tablet thickness.

- Friability test (FT):-

Five or two tablets of each formula were weighed and placed in a Friabilator (Mumbai, India) and rotated at 25 rpm for 4 min. The tablets were reweighed and the percent friability was then calculated according to the following equation:

%Friability = (Loss in weight/Initial weight)× 100.
% Friability = (initial weight – final weight) × 100
Initial weight

Friability is a measure of the tablets ability to withstand abrasion during handling. The friability test involves weighing a sample of tablets before and after subjecting them to mechanical shock. The formula for friability
Is:-
Friabilty(%) =

Initial weight – Final weight × 100
Initial weight

1. Initial weight :- weight of the tablets before the test.
2. Final weight :- weight of the tablets after the test.
3. Procedure:-

- **Instrument Method Image :-**

a) Weight a sample of tablets
b) Place them in the drum of the friability tester
c) Subject them to a specified number of rotations
d) Weight the tablets again.

In vitro disintegration time (DT):-

One tablet was placed in a beaker containing the time required for complete disintegration of the tablet was determined. In vitro DT for each formulation was carried out in triplicate and the results were expressed asmean ± SD.

The disintegration test is a Pharmaceutical quality control test to assess the time it takes for a tablets or capsule to break down into smaller particles. The general procedure involves placing a certain number of tablets into individual tubes and subjecting them to specified conditions, while monitoring the distribution time.

The formula for disintegration test (%Dt) is :-

Disintegration time :-Total time of the test

Formulations.
Graph:-
1. Collect data draw a graph.
2. Draw the graph coordinates Y and X Distintegration time and Formulations tested.

1) Weight machine for weight variation.

2) Vernier caliper for Thickness.

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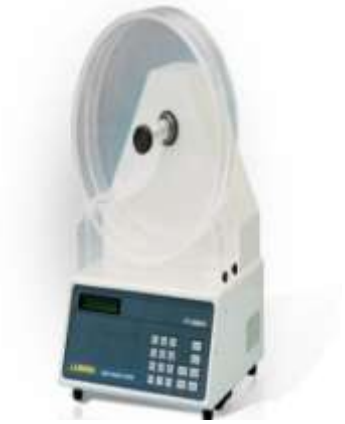
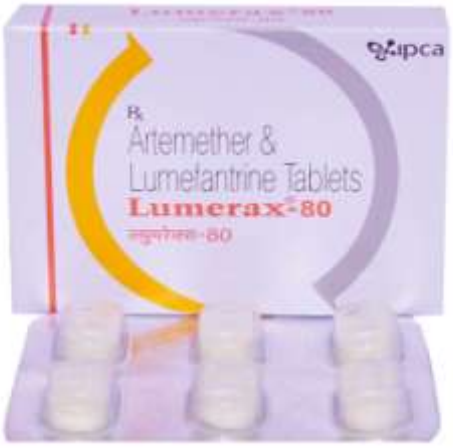
3) Disintegration tester.



4) Friability tester.

5) Hardness tester

❖ **The Brands product image A , B , C :-**



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❖ **Differences of all brand :-**

Brand name	Weight uniformity	Thickness	Hardness test	Friability test	Disintegration test
Brand A	± 41.26	3.140	e.g. 2.67 , 2.38 etc	1%	7.63 min.
Brand B	± 48.99	1.760	e.g. 3.97 , 3.12 etc	1%	7.60 min.
Brand C	± 56.95	2.26	e.g. 3.23 , 3.76 etc	1%	8.36 min.

Bioassay :-

❖ **Lumerax 80 –**

Uses –

Lumerax-80 tablet is used for the treatment of malaria cases not responding to other anti-malarial medicines.

Contradications –

If you are allergic to artemether and lumefantrine or any of the ingredients of the Lumerax-80 tablet. If you have a serious malarial infection with impaired body functions like difficulty in breathing, fits, kidney brain and liver-related problems. If you have a family history of heart disease. If you are taking medicines such as Flecainide, Metoprolol, Imipramine, Amitriptyline, Clomipramine, Terfenadine, Astemizole or Cisapride. If you have heart diseases like irregular heart rhythm or heart failure. If you have an imbalance of electrolytes in your body due to fluid loss.

Side effects –

- ❖ Nausea
- ❖ Vomiting
- ❖ Stomach pain
- ❖ Headache
- ❖ Cough
- ❖ Dizziness
- ❖ Fatigue
- ❖ Muscle or joint pain

Precautions –

- Lumerax-80 tablet is not recommended for use during pregnancy. However, doctors may give this medicine to pregnant women under critical situations where alternate antimalarial medicine is not able to treat the condition.

- For women who are using birth control measures (such as oral, transdermal patch or other systemic hormonal contraceptives), your doctor may advise you to take an additional non-hormonal method of birth control for about a month.

❖ **FM Plus –**

Uses –

This medicine is used for the treatment of malaria cases not responding to other anti-malarial medicines

Condraticitions –

If you are allergic to Artemether and Lumefantrine or any of the ingredient of this medicine If you have a serious malarial infection with impaired body functions like difficulty in breathing, fits, kidney brain and liver-related problems. If you have a family history of heart disease. If you are taking medicines such as Flecainide, Metoprolol, Imipramine, Amitriptyline, Clomipramine, Terfenadine, Astemizole or Cisapride. If you have heart disease like irregular heart rhythm or heart failure. If you have an imbalance of electrolytes in your body due to fluid loss.

Side Effects –

- ❖ Low appetite, vomiting, stomach pain, nausea and diarrhoea
- ❖ Headache, dizziness and sleeplessness
- ❖ Tingling or pricking sensation
- ❖ Unusual muscle movements, joint pain and fatigue
- ❖ Pounding and irregular heartbeat
- ❖ Skin disorders like rashes or itching
- ❖ Difficulty in walking properly and lack of energy
- ❖ Cough

Precautions –

This medicine has known to cause or suspected to cause harmful effects on the developing fetus, thus not recommended for use in pregnant women. However, doctors may give this medicine to a pregnant women under critical

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situations where alternate antimalarial medicine is not able to treat the condition.

❖ **Rezatrin Forte –**

Uses –

This medicine is used for the treatment of malaria cases not responding to other anti-malarial medicines.

Contraindications –

If you are allergic to Artemether and Lumefantrine or any of the ingredient of this medicine. If you have a serious malarial infection with impaired body functions like difficulty in breathing, fits, kidney brain and liver-related problems. If you have a family history of heart disease. If you are taking medicines such as Flecainide, Metoprolol, Imipramine, Amitriptyline, Clomipramine, Terfenadine, Astemizole or Cisapride. If you have heart disease like irregular heart rhythm or heart failure. If you have an imbalance of electrolytes in your body due to fluid loss.

Side Effect –

- ❖ Low appetite, vomiting, stomach pain, nausea and diarrhoea
- ❖ Headache, dizziness and sleeplessness
- ❖ Tingling or pricking sensation
- ❖ Unusual muscle movements, joint pain and fatigue
- ❖ Pounding and irregular heartbeat
- ❖ Skin disorders like rashes or itching
- ❖ Difficulty in walking properly and lack of energy
- ❖ Cough

Precautions –

- This medicine has known to cause or suspected to cause harmful effects on the developing fetus, thus not recommended for use in pregnant women. However, doctors may give this medicine to a pregnant women under critical situations where alternate antimalarial medicine is not able to treat the condition.

Therefore ,Lumerax 80 isbest brand or sustained release of Lumerax 80 tablet. Is used for the treatment of malaria in both children and adults. It contains two medicines both of which belong to a group of medicines called antimalarials. However, it is not used to prevent malaria or to treat severe/complicated malaria (when the brain, lungs, or kidneys are affected).

II. RESULT & DISCUSSION

All the samples used for the study were within their shelf life at the time of investigation. Three out of the eight brands of the **"Comparative analysis of Three brands of Artemether with Lumefantrine tablets"**have not been registered by NAFDAC. The results of the physicochemical properties of the various brands of **Artemether with Lumefantrine**are presented in Table . All brands showed acceptable uniformity of weight as none had percent deviation in weight greater than 5% as stipulated by the Indian Pharmacopoeia 1986. The significance of this test is to ensure that the tablets in each Lot are within the appropriate size range. The crushing strength of the tablets is an essential criterion in the determination of the ability of the tablets to resist chipping, abrasion or breakage under conditions of storage, transportation and handling before storage. The results showed that the brands examined had mean crushing strength within the range of 7.8 - 15 kgF. Another tablet property related to crushing strength is friability, which is designed to evaluate the ability of the tablet to withstand abrasion during packaging, handling and shipping. For compressed tablets, percentage loss in weight of less than 1% is usually considered acceptable. The results showed that brands A, B , C conformed to the required standard for friability, while brands D , E failed to comply. This failure could have resulted from the use of inadequate or insufficient amount of binding agent during formulation, inadequate moisture content during compression or insufficient compression pressure during tableting. The disintegration test measures the time required for tablets to disintegrate into particles. The BP 1998 stipulates a disintegration time of not more 15 min for uncoated tablets. The results of the disintegration test are presented in Table . The results showed that all the brands passed the disintegration test. The results of the assays of chemical

content to determine the amount of **Artemether with Lumefantrine**present in each formulation are presented in Table . They showed that all the brands contain between 90% and 110% of the labelled amount specified for **Lumefantrine**. There was no statistically significant difference between the different brands of the drug and

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theinnovator product, A. Furthermore, all the brands of the tablets except brand A passed the test for the content of **Artemether**The**Artemether**content of brand A was 141.2% which was significantly different from the innovator product, A ($p < 0.05$). This could be due to poor preparation techniques during formulation and subsequent manufacturing. An important character of powders during mixing is segregation, which occurs due to differences in particle size. Furthermore, the amount of**Artemether**inthe combination tablet is relatively small (i.e. 25 mg), which means any demixing or segregation during processing will result in non-uniformity of content.

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