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COMPARATIVE EVALUATION OF QUALITY CONTROL PARAMETERS OF METFORMIN (ANTIDIABETIC) TABLETS OF DIFFERENT MARKETED FORMULATIONS

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ABSTRACT
To assess and compare the bio-equivalency of six distinct metformin tablet brands. To conduct comparative analyses comparing the physiochemical characteristics of the pharmaceutical equivalency drug product and the therapeutic equivalency drug for the respective refer to the medications on the list. To guarantee the tablet's potency, efficacy, stability, acceptability by patients, and compliance by patients. To verify if a pharmaceutical tablet meets the necessary requirements to be labeled as a high-quality medication or not. To verify whether the quality parameters fall within the acceptable bounds.

INTRODUCTION
To guarantee therapeutic equivalency between a pharmaceutically equivalent test medicine and a generic or reference drug, bioavailability and bioequivalence tests are necessary. Maintaining consistency in pharmaceutical quality, efficacy, and safety standards products is the central pharmaceuticals standard control organization's primary duty (CDSCO). When determining whether distinct products with active substances offered by different licensees are interchangeable and clinically similar, bioequivalency must be taken into account.

Bioavailability and bioequivalence data, which primarily address the drug's release from the pharmaceutical dosage form and subsequent absorption into the systemic circulation, should be provided with applications for novel medications submitted under schedule Y.

It is commonly believed that human pharmacokinetic in vivo studies are the "gold standard" for evaluating immediate-release (IR) solid oral dosage forms' product bioequivalence (BE). But upon closer examination of this broad premise, it seems that in vitro research are better than in vivo research at times when evaluating the BE of IR solid oral dose formulations. In vitro studies have the potential to be superior in some situations due to their ability to: (a) lower expenses; (b) more immediately assess product performance; and (c) provide advantages with regard to ethical considerations.

Avoiding in vivo investigations when BE is obvious, when biopharmaceutics' data predicts BE, and when in vivo BE research type II results in lower expenses mistake rate is high. Because in vitro studies concentrate on comparing drug absorption from the two products, they provide a more direct assessment of product performance than standard human pharmacokinetic BE studies. On the other hand, because in vivo BE testing uses an indirect technique, it may present certain challenges. In vitro research can expedite development while adhering more closely to the ethical precept that "No unnecessary human testing should be performed."

Quality control tests for tablets
A little portion of quality assurance (QA) is quality control, which deals with sampling, testing, and documentation both during and after manufacture.

The monitoring procedure is how the manufacturer determines the real quality. performance, assesses it against benchmarks, and determines the reasons behind standard deviations to guarantee a high-quality output each and every time.

Generally speaking, quality control pertains to a process or series of actions carried out during a product's manufacturing to guarantee that it satisfies specifications and can be replicated.

Tablets are a solid dosage form for medications, either with or without excipients, that are made by molding or compression and are meant to be taken orally for both local and systemic effects. They could differ.

Linearity

If an analytical method can yield test findings that are exactly proportional to the concentration (amount) of the analyte in the sample, within a given range, it is considered linear.

The precision of an analytical procedure is defined as the degree of scatter, or closeness of agreement, between a set of measurements made by repeatedly sampling the same homogenous sample under prescribed conditions. The precision can be assessed at three different levels: repeatability, intermediate precision, and reproducibility. Research on precision is best done using real, homogeneous samples. However, in order to obtain a homogenous sample, it might be necessary to use synthetic samples or sample solutions; if this is not practical, then alternative research options might be taken into account. Standard deviation, often known as variance,

Intermediate precision

Variations within laboratories, such as various days, different analyzers, and different equipment, are expressed as intermediate precision.

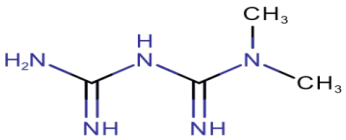
Accuracy

The degree of agreement between the values found and those that are recognized as either a conventional true value or an acceptable reference value is what determines an analytical procedure's accuracy. This is referred to as trueness at times.

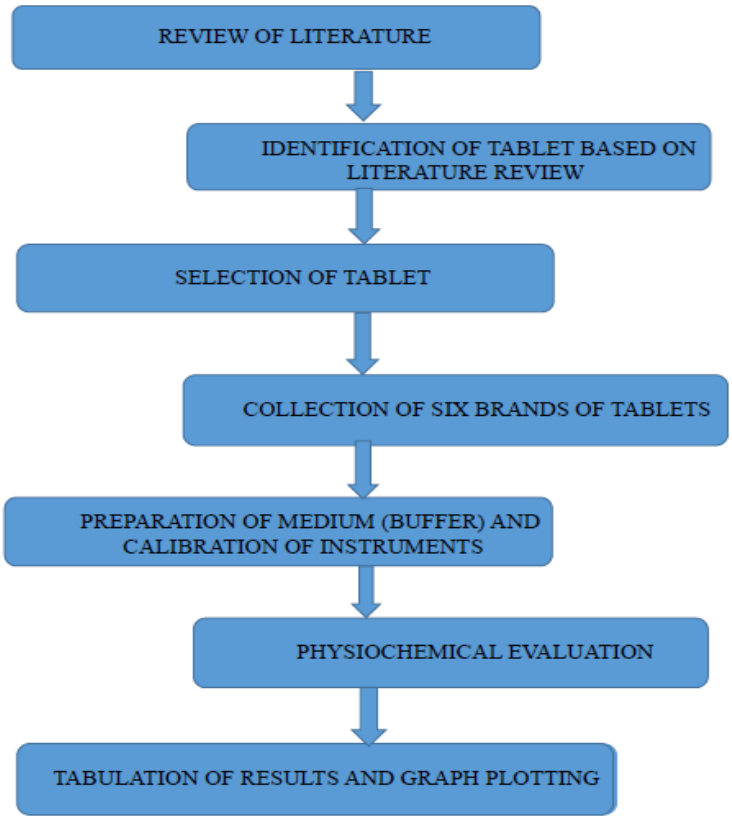
Repeatability

The capacity to transmit accuracy across a short distance while maintaining the same operational parameters is known as repeatability. Repeatability can also be referred to as intra-assay precision.

Drug profile

Drug profile	Properties
Synonyms	Metformin HCL
Molecular structure	
Molecular weight	129
Molecular formula	C4H12CLN5
Iupac name	N, N-Dimethyl imido dicarbonimidic diamide
Water solubility	1.38 MG/ML (Freely soluble)
Pka	12.33
Hydrogen acceptor count	5
Hydrogen donor count	4
Refractivity	56.64 M3·MOL-1
Melting point	223-226 ºC
Boiling point	224.1ºC
Polarizability	13.43 Å3
Volume of distribution	The apparent volume of distribution (v/f) of metformin after one oral dose of metformin 850 mg averaged at 654 ± 358l.24
Protein binding	Metformin is negligibly bound to plasma proteins
Absorption	The absolute bioavailability of a metformin 500 mg tablet administered in the fasting state is about 50%-60%.
Half-life	The elimination Half-life of metformin is 6.2 hours in the plasma
Clearance	Renal clearance is about 3.5 times greater than creatinine clearance
Mechanism of action	metformin decreases blood glucose levels by decreasing hepatic glucose production, decreasing the intestinal absorption of Glucose and Increasing insulin sensitivity by increasing peripheral glucose Uptake and Utilization.

Plan of work



MATERIALS AND METHODS

Hardness test

Tablets that are solid are arguably the most often used medicine dose form. Tablet hardness is a useful metric for quality control as well as a benchmark to direct product development. Tablets shouldn't be overly soft or firm. Tablets that are very hard could mean that there is too much binding force between the active ingredient and the excipient, which could be preventing the tablet from dissolving properly and preventing the necessary dose information. In a similar vein, insufficient binding could lead to softer pills that dissolve too soon when swallowed by patients.

Thickness test

One of the most popular and often utilized tests for tablets that is carried out throughout the tablet compression process is the thickness test. After line clearing, a tablet thickness test is first carried out to make sure that each tablet's thickness falls within the range stated in the BMR. Later, the thickness of each tablet is tested at predetermined intervals during the compression process. The sole dimensional variable associated with the tablet compression process is the tablet's thickness. It is typically measured with a micrometer.

Friability test

Tablets are tested for durability during packing and transportation using a procedure called friability testing. This entails employing a revolving drum with a baffle to drop a sample of tablets repeatedly over a predetermined amount of time. The proportion of tablet mass lost due to chipping is determined and any broken tablets are examined in the outcome.

Weight variation

To verify that each tablet has the specified amount of metformin, a weight variation test was performed. A digital balance was used to weigh twenty pills as part of the test. Milligrams were used to compute the average weight. The weight variation test, according to the USP, is conducted by weighing each of the twenty tablets separately, figuring out their average weights, and then comparing those weights to the average.

Disintegration

A pharmaceutical technique called disintegration testing was created to assess and determine whether or not a pill or sample breaks down in the human body, and whether it does at all. This test should not be confused with dissolution, which is the disintegration process that comes just after. The effectiveness of a sample's disintegration from its produced form into smaller, looser, more freely flowing structures that can subsequently combine to create a solute with the liquid it has broken down in is assessed by disintegration tests. To put it simply, the disintegration test determines whether the sample breaks down into a powder or stays in the form of a solid tablet block.

Dissolution

The degree and pace of disintegration can be determined with the use of dissolution testing. It influences the drug's bioavailability and absorption. The USP type II apparatus was used to conduct the dissolution test. 6.8 grams of potassium dihydrogen phosphate were dissolved in 1000 millilitres of water to create the dissolution medium, which is a 0.68% w/v solution of potassium dihydrogen phosphate. One tablet was inserted to the dissolving basket, which was set within the 900 ml dissolution medium-filled dissolution jar. The instrument was rotated at 100 rpm for 45 minutes while the temperature was kept at 37 ± 0.5°C. A graph was constructed after 1 ml of the sample solution was left in a jar for 45 minutes and the resultant absorbance was recorded. The solution's maximum wavelength of 233 nm was noted.

Drug release kinetic study

The model-dependent technique was used to do the kinetics, and different kinetics, such as zero order, first order, Higuchi's, and Korsmeyer-Peppas models, were applied to the formulation's dissolving profile. Plotting of the data from in vitro drug release investigations was done using a variety of kinetic models; zero order (Equation b) shows the cumulative amount of drug released over time. Higuchi's model (Equation 3) ns cumulative percentage of drug released against square root of time, and first order Equation 2) as log as cumulative percentage of drug remaining vs time.

Qt= Q0+k0t (Equation 1)

where k0 is the zero-order rate constant expressed in units of concentration/time and is the time in hours; Qt is the amount of drug dissolved in time t; Q0 is the initial amount of drug in the solution. Concentration vs. time plotting would result in a straight line that intercepts the x axis origin and has a slope of k0.

LogC= logC0-kt/2.303 (Equation 2)

where t is the time, Co is the drug's starting concentration, and is the first order constant.

Qt= KHt1/2 (Equation 3)

where tis is the time in hours and KH is the constant representing the system's design variables. The reciprocal of the square root of time is therefore proportional to the medication release rate. The exponent n was determined by calculating the slope of the straight line when drug release was plotted as log cumulative percentage of drug released vs. log time in the Korsmeyer equation.

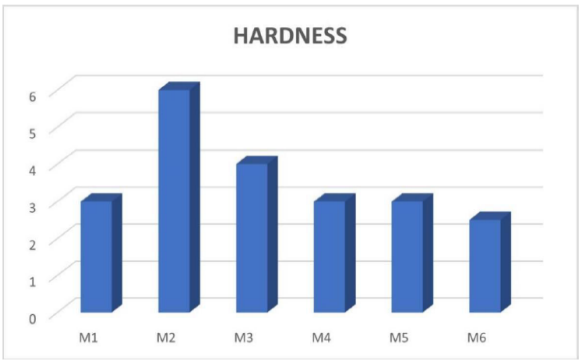
$Mt/M_{\infty}= Kt^{n}$ (Equation 4)

where t is the release time and Mt/M∞ is the fractional solute release. One kinetic constant is K.

RESULTS

Hardness

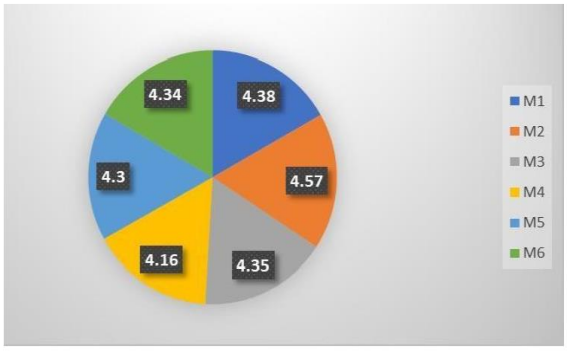
Acceptance criteria for Hardness of tablet- ±0.5mm



Hardness graph

Thickness

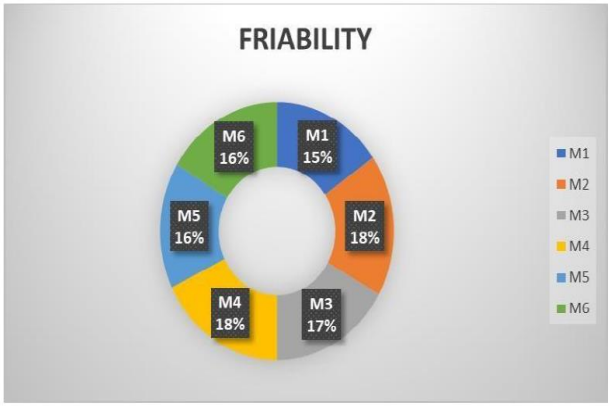
Acceptance criteria for Thickness of tablet – 0.5%



Thickness chart

Friability

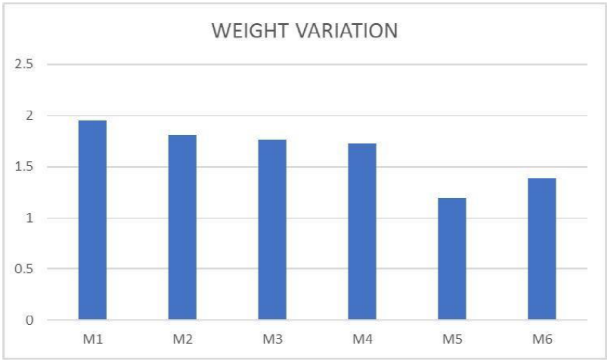
Acceptance criteria for Friability of tablet - Not more than 1.0%



Friability chart

Weight variation

Acceptance criteria for Weight variation of tablet - 5%

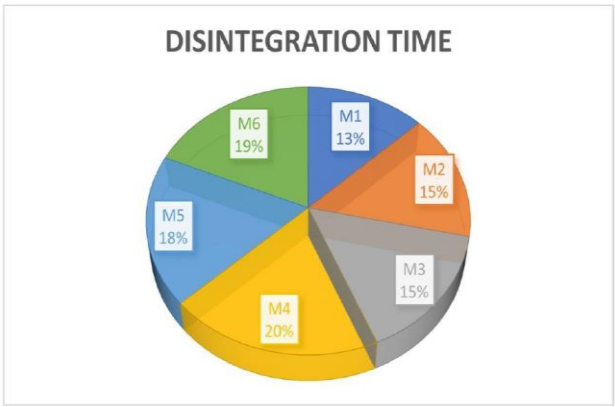


Weight variation graph

Disintegration

Acceptance criteria for Disintegration Time of tablet - Not more than 10%

S. No.	Brand name	Disintegration time (M/S)
1	M1	4.32
2	M2	5.07
3	M3	5.04
4	M4	6.47
5	M5	6.00
6	M6	6.15

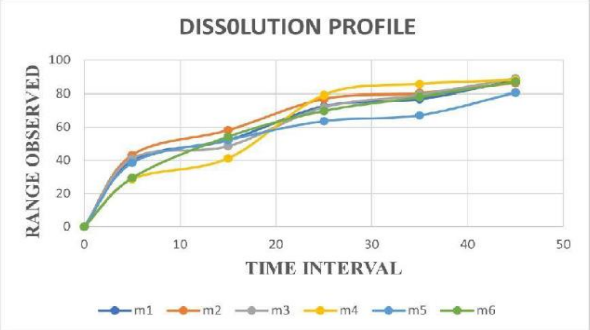


Disintegration chart

DISSOLUTION

Acceptance criteria for Dissolution of tablet - Less than 15min

Time (min)	M1 (%)	M2 (%)	M3 (%)	M4 (%)	M5 (%)	M6 (%)
5	40.12	43.24	41.23	28.56	38.45	29.35
15	52.71	58.12	48.62	41.16	52.71	54.24
25	72.68	76.92	72.02	79.19	63.61	69.84
35	76.83	80.23	79.45	85.65	67.67	78.13
45	87.81	86.12	89.12	87.94	80.63	87.02



Dissolution profiles of different formulations

CONCLUSION

There are several generics of Metformin tablets available within the drug delivery system in India. The increasing level of use of Metformin tablets in the clinical practice creates the need to monitor and quality control assessment and for purpose of generic substitution. All the product have satisfactory result in respect of uniformity of weight, hardness test, friability test, and thickness, disintegration, and dissolution profile. Every test related to the evaluation of Metformin 500mg tablet was compiles according to USP and IP. The important quality characteristics of 500mg tablets IP are well defined and control. There are no outstanding quality issues that would have a negative impact on the benefit balance. The efficiency of these tablets was well established which leads the patient with no microbial contamination to get expected therapeutic effect. The comparative analysis of these tablets compiles with standards. We have compared all the tablet quality control study revealed that collected samples of Metformin 500mg tablets available in Tamil Nadu, India manufactured accordingly to cGMP as well as another standard monographs.

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