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Original Article

Study the effect of local brands of Clomiphene citrate in comparison with the standard brand of similar generic

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ABSTRACT

For the evaluation of the drug quality there is a method of a comparative study in which a drug of different brand with similar generic is collected and different tests were performed to check about the difference and similarity between them related to their size, activity and price. In this study we evaluate the quality of the uncoated tablet of generic Clomiphene citrate "X" brand that is standard with the other two local brands i.e "Y" & "Z". These medicines were brought for our comparative studies and we performed different tests to check the differences with respect to their quality. The tests which were perform followed the procedures given by the Standard British Pharmacopeia, include, Hardness test, Friability test, Dissolution test for the quality monitoring of post formulation and for the tablet design, we observed that in hardness and friability test there is no variation between the drugs. On the other hand, in dissolution or disintegration test we observed a considerable variation of sample "X" as compare to sample "Y" and "Z", such that after this study work we can conclude that tablet of brand "Y" is more reliable as compare to the standard brand "X".

Key words: Clomiphene citrate, comparative, Hardness, Dissolution

INTRODUCTION

There are many different drug formulations present such as suspensions, emulsions, solutions, elixirs, syrups, if they are of 5-30ml then they contain one dose of medication but because of the factor that is arrive when the patient self-administered the drug these doses are erratic. There is also a unit dosage form of medication present that is Capsules and Tablets. [1] [2]

All these formulations have a different route of administration which alter the effect of the drug such as parenteral route through which insulin therapy is given and it also gives the fast action as compare to other routes, a topical route in which we applied nitroglycerine for the treatment of scopolamine and angina but because of systemic action of drug it lacks effective absorption of drug, an oral route through which we have a systemic effect of drug in patient's body [3][4] and this is the preferred route for drug administration. Tablets and

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capsules are the type of formulation which is given through oral route for drug administration, but the tablet has many advantages over other formulation as it is a type of dosage form which is tamper proof [5-6] and for the quality assessment of any medication we can perform different types of quality control standard test on tablet such as uniformity of weight, diameter, shape and size of a tablet, friability, hardness, dissolution, disintegration and percentage assay of a drug [7-9]. Clomiphene is a medicine used for fasten the process of ovulation or to treat infertility in women. It basically increases the release of that hormone that support the process of ovulation. This medicine is contra indicated in females with primary pituitary or ovarian failure [13].In this study we took a standard and other two local brand of tablet dosage form with similar generic and perform Hardness, thickness, size & shape variation, friability and thickness tests and compared the standard brand with other local brand to study the effect of drug composition in release rate.[10-16]

MATERIALS AND METHODS

Material: Quality control test of clomiphene citrate uncoated tablet of 50mg were taken by collecting the tablet of different brands for the purpose.

Equipment: Friabilator, Electronic balance, UV spectrophotometer, Disintegration apparatus B.P standard, Hardness tester, Dissolution apparatus, Vernier calliper

Chemicals: Distilled water

Evaluation of clomiphene citrate tablets: The tablets were evaluated for following parameters;

a) Appearance
b) Weight variation
c) Thickness
d) Friability
e) Disintegration time
f) Dissolution
g) Hardness
h) Assay
i) Drug content [17]

Methods:

Thickness: By following the specification of pharmacopeia, 20 tablets were taken from each sample to measure the thickness with the help of Vernier caliper [12].

Weight variation test: For the weighing test, calculate the standard deviation and average weight by taking the weight of 20 tablets from each formulations by using analytical balance [5].

Hardness Test:

- The strength is the property which helps to hold off the tablet when the strain or stress applied to it, this phenomenon is known as hardness.
- The hardness of the tablet can be determined by using hardness tester where the tablet has to be placed in between the movable and fixed jaws and the pressure will be applied by the screw knob. The pressure is increased gently at the edges of the tablet to break it. Scale tells the reading that how much pressure is applying on the tablet which is going to break it.
- Hardness of the tablets is depending upon the spaces between the lower and upper punches during compression, material weight, pressure on compression, quality and the nature of the excipients.
- If the tablet as a finishing product is too hard then it will harder to disintegrate fast and if it is too soft then it will break easily during transportation and packaging [9].

Friability test:

- The property of the tablet which hold off the tablet against abrasion during packaging, transportation and handling is known as friability and the test to evaluate this property is known as friability test.
- Friabulator consists of chamber made up of plastic is divided into 2 parts and it revolves at 25 rpm. Tablets with fixed number are weighted first and then put them into tumbling chamber which rotates 100 revolutions for 4 minutes. Each rotation gives a fall to the tablet from a distance of 6 inches to undergo shock. After the 100 revolutions again evaluate the weight of each tablet, the weight loss shows friability.
- Loss in weight should not be more than 0.8%t.
- The friability (f) is shows as: f=100 (1-wo/w),
- Where, wo = initial weight before friability of the tablets and w = weight after friability of the tablets [10].

Disintegration Test: To perform disintegration test of tablets, take 6 tablets from each formulation and put them in the apparatus. The disintegration medium volume is about 900ml of water is maintained at 37± degree Celsius. The time When the tablet is broken into small pieces and pass from the screen will be noted and evaluate the average time [5].

Dissolution Test: Fill the dissolution medium with stated volume, then apply the dissolved air in vessel of apparatus. Heat the dissolution medium between 36.5degree to 37.5 degree. The tablet goes

down at bottom of the vessel before the paddle start to rotate. To keep the tablet at horizontal position helix wires are being used which prevent the floating of tablet in bottom of vessel. From the surface of the tablet air bubbles are removed. Withdraw the sample from the surface of dissolution medium and evaluates the absorbance under spectrophotometer. The procedure is rerun 5 times and evaluate the amount of active ingredient is dissolve as a percentage [11].

Assay: The technique which is very efficient in the pharmaceutical analysis is UV visible spectrophotometry It is used to determine the amount of ultraviolet and radiation by the substance in solution. UV visible spectrophotometer is used to determine the ratio, intensity of 2 beam of light in UV visible region and ration function. For our standard drug of clomiphene citrate that is "X" we check absorbance at wavelength of 298 lambdas in UV spectrophotometer. Beer lambert law states the qualitative spectrophotometric analysis [6]. It is used to determine the amount of substance present in a solution [5].

Content uniformity:

- For oral dosage form, it is an important estimation. It Is used to check and estimate the dosage unit uniformity. The consistent dose of API is assured and maintain between the number of batches and assure that the patient is taking correct dose. It also ensures that the active ingredients are distributed evenly in the whole tablet so that if it is broken into two, both halves contain the half of the dose.
- 10 tablets are weighted first and then powdered to check the content uniformity test. The quantity of powder should be equal to 50mg of clomiphene citrate in water. For checking content uniformity, evaluate absorbance in dilution with water. Curve shows the content uniformity. The content of medicine can be determined by taking average of 3 readings [8].
- The content uniformity can be determined by: Absorbance of sample/ absorbance of standard × 100 [12]

Standard preparation: For the preparation of 500 ppm, take 50mg medicine and make it dissolve in the volume of 100ml distilled water. With draw 10ml of solution and make the volume up to 100 ml with water.

Test Preparation: Take 10 tablets and allow them to weight it first and powdered them. The powdered tablet should be equal to the 50mg of clomiphene citrate. then again weight the medicine and place it in volumetric flask which has 100ml graduation, add some amount of water to dissolve the powder by shaking. After adding distilled water, makeup the volume up to 100 ml. take 10ml from the 100ml solution and again makeup the volume with water up to 100ml [7].

Observation: Between the 250nm to 330 nm scan the standard solution in UV spectrophotometer, where water is used as a blank. Clomiphene citrate give the maximum wavelength is 293

RESULT AND DISCUSSION

In our present study, tablets of clomiphene citrate of three different pharmaceutical companies 'X', 'Y' and 'Z' were used. There is a same active in all the three drugs but they may differ because of a little change in their composition. Standard procedures or test like hardness, friability, dissolution rate, disintegration, content uniformity, and assay of the tablets have been performed in our study as mention earlier. Using the experimental observations, various plots have been drawn.

Table 1: QC tests of clomiphene citrate standard and other brands

S.No	Sample 'X'	Sample 'Y'	Sample 'Z'
Appearance	Light Yellow color, Rounded-diamond shape, smooth, free from cracks	White color, Rounded-diamond shape, smooth, free from cracks	White color, Rounded-diamond shape, smooth, free from cracks
Color	Light Yellow	White	White
Taste	Bitter	Bitter	Bitter
Thickness (n=10)	3.53mm	4.61mm	3.31mm
Diameter	9.61mm	9.66mm	8.77mm
Hardness (n=10)	69 N	170 N	63 N

Weight (n=10)	303.5mg	284mg	196.2mg
Disintegration (n=2)	13min 37sec	4min 7sec	6min 41sec
% Assay	100%	84.8%	94.2%
Content Uniformity	100%	81.6%	33.3%

"As mention above there is only a slight variation between the tablets in hardness test and the disintegration time of standard "X" differ from the other two local brand "Y" "Z" as there may be a difference in the presence of excipients between them".

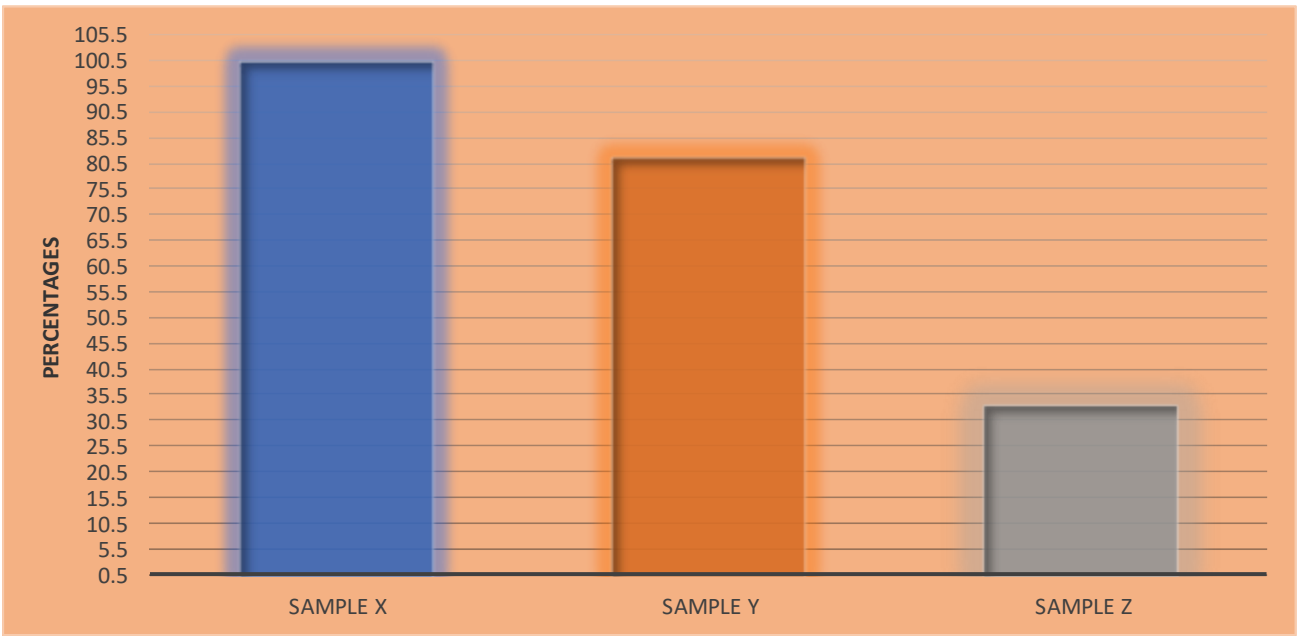

Figure 1 :Above mention graph show the Pecentages of all the three brands that is "X", "Y", "Z".

CONCLUSION

In this research we observed that in hardness and friability test there is no variation between the drugs. On the other hand, in dissolution or disintegration test we observed a considerable variation of sample "X" as compare to sample "Y" and "Z", such that after this research we can conclude that tablet of brand "Y" is more reliable as compare to the standard brand "X". Finally quality control parameters are related to one another from initial step to pharmacological action of the drug, a high-quality tablet either single or in combination should meet all the standard quality parameter for getting its desired therapeutic response.

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