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PHARMACEUTICAL EVALUATION AND COMPARISON OF VARIOUS BRANDS OF PARACETAMOL TABLET FORMULATION.

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ABSTRACT

Objective: To compare the quality of the paracetamol tablet formulation manufactured by various multinational companies and local companies with international standards
Materials and methods: The tablet formulations of ten different brands manufactured by MNC and local companies were tested for various parameters like hardness, friability, disintegration time, dissolution time, sedimentation, pH and dry weight using standard techniques .the values were compared with the standards.
Results: Wide variations in the parameters were seen in the tablet formulation manufactured by the local companies, where as the formulations manufactured by the MNC were comparable with standards.
Conclusion: The manufacturing standards are not strictly followed by the local companies and there is need for proper monitoring.

KEYWORDS: Paracetamol, Hardness, Friability, Disintegration Time, Dissolution

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INTRODUCTION

Medical sector in the present world has changed into a therapeutic jungle.[1] pharmaceutical companies are competing among themselves to bring out new molecules for different ailments.[2] A single generic drug is manufactured by different companies under different brand names. In India drugs are also manufactured by small scale sectors which may be widely distributed or locally marketed. Drugs especially for the common ailments are available as over the counter.[3] It has found in several studies that the majority of the drugs are being consumed without proper prescription especially in rural areas.[4] Many of the small scale sector pharma companies may or may not follow the international standards in the drug manufacturing process.[4] So there is need for proper quality control of the drugs. The same can be done by qualitative and quantitative analysis of the drug formulation. Hypothetically speaking a single generic drug even though manufactured by different companies under different brand names, should match in the pharmaceutical parameters[2,5] . Variation in the pharmaceutical parameter is mainly due to variation in the manufacturing process[3].These variations have a definite impact on the therapeutics of the drug, ie the drug may not provide the expected result[3].Use of counterfeit and substandard drugs bear serious health implication; such as treatment failure and adverse reactions.[6] A drug formulation (especially tablet, capsule etc) when consumed orally first disintegrate then gets dissolved in the secretions and finally absorbed into the systemic circulation[1]. The various processes which a drug undergoes inside the body is studied externally using various equipments. Important parameters studied are weight variation, hardness, friability, disintegration, dissolution and pH of the drug.[5,7] Hardness of the tablet is strength of the formulation it is assessed as the force or weight required to break the tablet, in simplest words it is the crushing strength.[5] it is measured in kilograms and is the force required to break a tablet. Oral tablets have a hardness of 4 to 10 kgs, hypodermic and chewable tablets have hardness of 3 kgs and that of sustained release tablet is 10 to 20 kgs. Friability is defined as percentage of weight loss of the drug due to mechanical action.[3] Tablets are constantly subjected to mechanical strokes and aberration during the process of manufacturing, packaging and transportation process. Friability refers to ability of the compressed tablet to avoid fracture and breakage during transport. It is closely related to hardness and is measured by using Roche fibrillator or tambler test.[9] Disintegration is defined as the state in which no residue of the tablet or capsule, except fragments of the undissolved coating or capsule shell, remains on the screen of the test apparatus or, if any other residue remains, it consists of soft mass having no palpably firm, unmoistened core.[10,11] Dissolution is considered as one of the most important quality control test. The transfer of molecules from solid state into a solution is known as dissolution, it describes the process by which the drug particles dissolve.[12] It is a rate limiting step in the absorption process and a tool for predicting the bioavailability and to determine bioequivalence. There is a direct relation between dissolution rate and bioavailability of the drugs and therefore it can be a useful guide to comparative bioavailability. Disintegration plays an important role in dissolution process. Hardness of the formulation has an effect on disintegration process which in turn affects the dissolution process. Dissolution in turn affects the bioavailability of the drug, which in turn governs the therapeutic effect.[13] Each of the parameters is interrelated with each other hence the above parameters were considered in our study. Paracetamol or acetaminophen is a NSAID-non steroidal anti-inflammatory drug is used commonly for relief of fever and pain.[14]

MATERIALS AND METHODS

In the present study ten different brands of paracetamol recently manufactured and same

manufacture date were used. For convenience the drugs were divided into two major groups, first group consisting those manufactured by the multinational companies and while the second group was those manufactured by local companies. In each group five different brands were tested, the dose of the drug was kept constant. The names of the manufacturer are not mentioned for legal purpose. Pharmaceutical evaluation of the drug was done using following parameters[2,9]Weight variation among the tablets Hardness of the tablet Friability of the tablet using friability test Disintegration time of the tablet using disintegration apparatus Dissolution time where the preparation gets converted into a solution after which the pH is also noted using the digital pH-meter. Identification test for the presence of paracetamol.[2] Weight variation was used to show the uniformity of content of the tablet. Hardness of the tablet is maximum load a tablet can sustain before it breaks. The principle of measurement involves subjecting the tablet to an increasing load until the tablet breaks or fractures. The load is applied along the radial axis of the tablet. Friability test is used to test the friability of the tablet; a number of tablets are weighed and placed in the apparatus where they are exposed to rolling and repeated shocks as they fall six inches in turn within the apparatus. After 4 minutes of this treatment or 100 revolutions tablets are weighed and the weight compared with initial weight.[2,3] The loss due to abrasion is a measure of tablet friability. The value is expressed in percentage. Tablet disintegration is done using the disintegration apparatus.[5] Tablet disintegration machine manufactured by INCO labs was used for the study of the disintegration process. The apparatus consists of circular basket assembly a suitable vessel for the immersion fluid (such as 1 litre beaker), a thermostatic arrangement for maintaining the fluid at a required temperature (37^{o}c) and a device for raising and lowering the basket –rack in the immersion fluid at a constant frequency of 28-32 cycles/min through a distance of 50-60 mm. The basket rack assembly consists of six open ended cylindrical glass tubes and a rack for holding them in a vertical position. Details of equipment are explained.[2,5] Drop the tablets on to the mesh screen and record the time needed for tablets to disintegrate. A reasonable disintegration time should be between 15 to 30 minutes although the time will depend upon the product and stirring speed etc. Dissolution apparatus assembly is used to record the dissolution time.[11] Percentage of dissolution of the drug at the end of 60 min was taken into consideration and was measured by UV double beam spectrophotometer.[12] pH of the solution analysed using a digital pH meter.[9]Identification test: 0.5 g of paracetamol were extracted with 20 ml of acetone, filtered and evaporated. The filtrate was dried at 105^{o} c with drying oven.0.1 g of the dried residue boiled with 1 ml of HCl for 3 minute and 10 ml of water were added and cooled. It was observed whether precipitate was formed or not. Then, 0.05ml of 0.0167 mole of potassium dichromate was added with micropipette to see the appearance of violet color.[2]

RESULTS

The results obtained are tabulated as below:

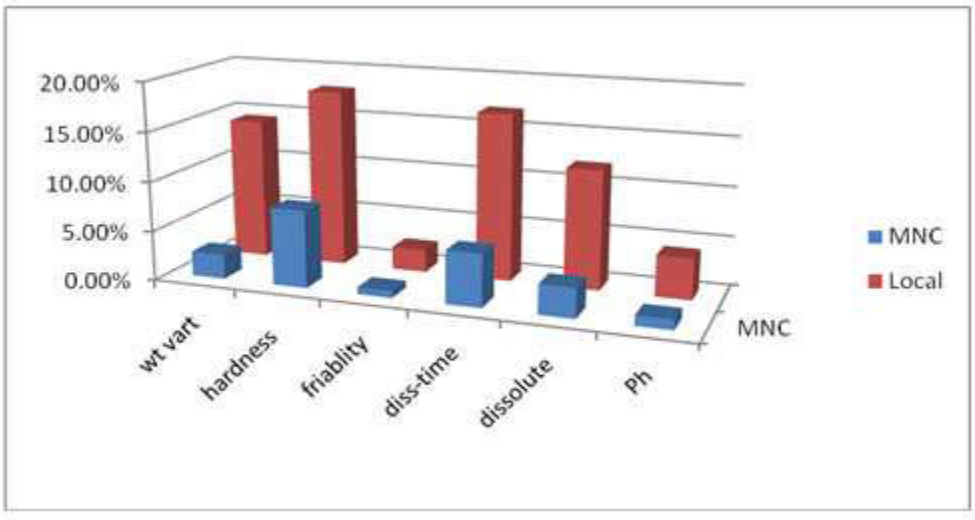
Table 1
Variations in the different parameters of different brands of paracetamol

Sl.No Brand	Weight variation	Hardness	Friability	Disintegration Time	Dissolution After 60m	pH	Identification test
STD	600 mg	7 kg	1%	10 min	100%	7	++
MNC							
1	610	7.25	0.76	9 m-30s	98%	7.10	++
2	625	7.50	0.43	9m-20s	100%	7.05	++
3	590	6.75	0.66	9m-30s	95%	6.95	++
4	610	7.75	0.76	9m-10s	100%	7.10	++
5	580	7.50	0.84	10m-10s	90%	6.95	++
Avg	603	7.35	0.69%	9m-32s	97%	7.03	++
Local							
1	500	8.25	4.32	13m-20s	80%	6.75	+
2	650	6.25	0.97	12m	90%	7.35	+
3	450	7.25	2.57	8m-20s	85%	7.25	++
4	650	5.75	2.72	9m-30s	95%	6.60	++
5	520	5.25	0.98	11m-20s	90%	7.20	+
Avg	554	6.55	2.312%	10m-54s	88%	7.03	+

Table 2
Mean deviation and %deviation of various parameters:

Parameters	STD (standard)	MNC (multi national company)	Mean Deviation from STD	%	Local	Mean Deviation from STD	%
Weight variation	600mg	603mg	15mg	2.5%	554mg	86mg	14.34%
Hardness	7 kg	7.35kg	0.55kg	7.85%	6.55kg	1.25kg	17.95%
Friability	Up to 1%	0.69%	--------	0.69%	2.312%	---------	2.312%
Disintegration Time	10 min	9m-32s	32 sec	5.33%	10m-54s	1m-50s	16.875%
Dissolution Rate (after 60m)	100%	97%	3%	3%	88%	12%	12%
pH	7	7.03	0.07	1%	7.03	0.29	4.142%

Graph 1
Variation in different parameters of MNC and local brands of paracetamol.



Weight variation
Local manufactures did not give much importance to weight of tablet, there was variation of up to 15% while in case of MNC was only 2.5%.

Hardness
The tablets manufactured by the multinational companies did not show much difference in the hardness, while those manufactured by the local companies showed wide variation. Some of the brands were softer and some much harder when compared to the standard values.

Friability
Almost all the tablets when subjected to the friability test showed friability. But the overall friability was more in the locally manufactured tablets when compared to those manufactured by MNC's .Also the fragments were large in locally manufactured tablets.

Disintegration time
Majority of the tablets disintegrated in the stipulated period of time. The disintegration time of the tablets manufactured by the MNC was almost same with standards. Among locally manufactured tablets, some disintegrated fast while some were slow to disintegrate. This variation was 16.875% which is comparatively more [2,5].

Dissolution
Because of direct relation between disintegration and the dissolution the dissolution process was affected proportionately[11]. Dissolution was better in drugs from MNC but the tablets from local companies also dissolved but took more time and showed lower consistency. pH of the solution had no much variation except in case of two of the brands of paracetamol manufactured by the local companies where the variation was more; this may have been probably due to the influence of binding agent. In the identification test all the brands of tablet showed the presence of paracetamol but the quality of test was poor in case of local tablets which may be because of lower concentration of paracetamol.

DISCUSSION

In the present study we have made an attempt to know the qualitative difference in the different brands of the paracetamol tablet formulation. Paracetamol is widely used antipyretic and anti-inflammatory agents. The drugs are also manufactured and marketed by innumerable companies which include both multinational and local companies. The study is simple and only compares the different parameters of different brands with standards. It can be easily carried out in a simple set up. The study can be improved upon by including quantitative analysis of the drug but this needs sophisticated equipments for the study. The study has attempted to compare the quantitative difference in the various ingredients of a formulation, but actual concentration of the drug needs to be evaluated. Well equipped laboratory consisting of sophisticated equipments like HPLC and gas chromatography is needed.[13] The study finds to be simple and is useful especially for monitoring the quality of the drugs available in the local market. Even though it cannot give accurate results, but can be used as initial vital tool to access the quality of the drugs. Paracetamol in high doses causes acute toxic effects in different tissues namely liver and also in purkinje cells of brain. [15] In the above study commonly used tablet formulations were tried but there is need of scope for evaluating the mouth dissolving formulation. A combination of six parameters weight-variation, hardness, friability, disintegration time, dissolution and pH of solution were assessed in the study. Small variations in one or two parameters are acceptable but a marked variation in multiple parameters highlights the defect in the manufacturing process of the drug.

CONCLUSION

The quality of the local brand of paracetamol was found to deviate much from standard when compared to those manufactured by the multinational companies. So there is need for proper control over the manufacture of substandard drugs.

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