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Pharmaceutical Stability of Brands of Paracetamol Tablets under Different Environmental Conditions

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ABSTRACT

Drugs are exposed to some conditions which are inevitable in the shelf-life of those drugs. Such conditions are met during drug distribution to the point of consumption. If stability of a drug product is not maintained throughout its shelf-life, quality, safety, potency and efficacy will be compromised. This study aimed to investigate the effect of these conditions on the pharmaceutical stability of paracetamol tablet formulations.

Three brands of paracetamol tablets were stored in their original packages under different environmental conditions (living room, kitchen, out-door and trunk of a car) for 24 months. Samples were withdrawn at different time intervals and evaluated for variations in weight, diameter, hardness, friability, content uniformity and disintegration and dissolution. One-way ANOVA and student t-test were used to compare difference in data.

Organoleptic properties of the tablets were maintained for the 24 months except the brands kept out-door which had an off white colouration. Drug degradation was minimal with the paracetamol packaged in PVC blisters. The pharmaceutical stability of the three products in the living room and in the kitchen at 24 months was not adversely affected while those kept out-door and in the trunk of a saloon car was adversely affected.

Keywords: Stability, environmental conditions, degradation, drug content, paracetamol.

Introduction

Drug stability is defined as the capacity of a drug substance or drug product to maintain its identity, strength, quality, and purity within official specification throughout its shelf life.[1] The stability of a drug product must have to be maintained throughout its shelf-life otherwise the quality, safety, potency and efficacy will be compromised.[2,3] All form of drug delivery system is subject to changes under the influence of some environmental factors such as light, humidity and temperature.[4-7] These changes could lead to deterioration and degradation usually as a result of oxidation, hydrolysis, photolysis, thermolysis, etc, thus making consumers at risk of some drug related problems ranging from suboptimal treatment, therapeutic failure, adverse reactions, toxicity, etc.[3,8-10]

The pharmaceutical changes that can occur to solid dosage forms (tablets) are; changes in tablet dimensions, weight, colour, hardness, friability, drug content, disintegration and dissolution. Environmental factors are unavoidable conditions which drugs will have to pass through during transportation, storage and use.[11-13] This is very essential in determining the integrity of these products. So, for stability to be maintained, these factors are of utmost importance and must be put under control. It has been reported by many authors that, stability is widely affected by external factors or environmental conditions.[14,15] Optimal storage conditions must be ensured throughout the drug distribution avenues to the point of consumption (Figure 1).

World Health Organization has an established guideline which addresses issues relating to drug stability with special focus on countries in the tropical climate zones [Zones III (hot and dry) and IV (hot and humid) according to W.H.O. classification] where drug stability constitutes a serious threat to drug product stability.[16] This is why drug stability test is a necessary procedure for registration of new drug substances and products during development as outlined by W.H.O.

In this study, three brands of paracetamol tablets were stored under some real time environmental conditions to investigate the effect of such conditions on the pharmaceutical stability of the paracetamol tablets.

Materials and Methods

Drugs and reagents

Three brands (P1, P2 and P3) of paracetamol 500 mg tablets manufactured in Nigeria were purchased and used for this study. P1 and P2 were available as PVC blister packaged while P3 was available as loose packaged in a wide mouthed plastic jar. All reagents used were of analytical grades.

Stability testing

The real-time stability testing procedure was adopted for this study by storing samples for twenty four months according to a modified W.H.O. guideline.[17] All three brands of paracetamol were within their shelf life. They were stored in their original packages under different environmental conditions (living room, kitchen, out-door and trunk of a car) for 24 months. Samples were taken and tablet parameters namely hardness, friability, disintegration, drug content etc. were evaluated at 0, 1, 3, 6, 9, 12, 18 and 24 months.

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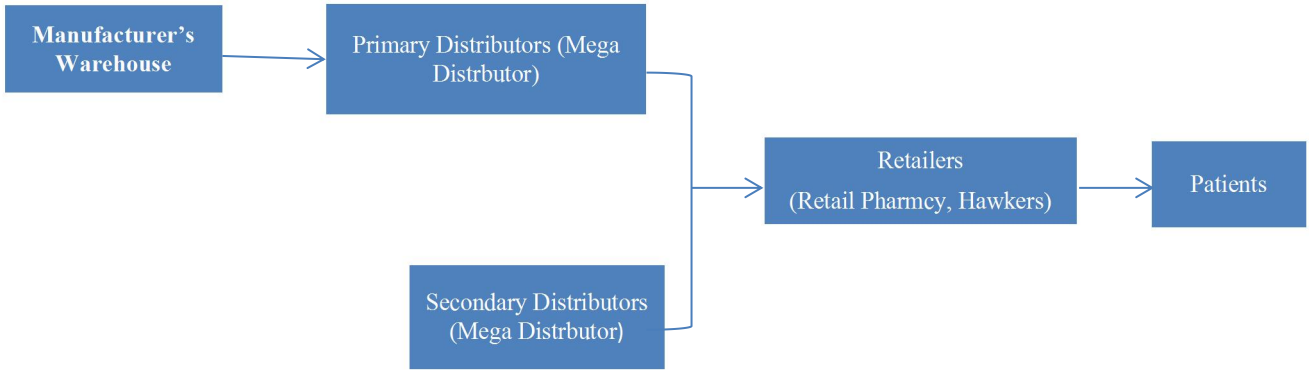

Figure 1: Drug distribution channels in Nigeria

Tablet Evaluation

The required number of tablets was withdrawn from the samples and exposed to different environmental conditions at specific time for evaluation of pharmaceutical parameters of the tablets according to USP[18] and the methods of Bele[19], Kalia *et al*.[20], Adeleye *et al*.[21], Jain and Naruka,[22] Gandhi,[23] Adeoye and Alebiowu.[24] Average of three determinations was taken for each of the evaluations. The tablets were also observed for colour and physical abnormal changes.

The individual and average weight of twenty tablets was noted for weight variation test. The thickness and diameter of individual tablet was measured using a micro-meter screw gauge. The force required to split the tablets diametrically using a hardness tester (DKB instrument, Mumbai. Model EH 01) was measured and expressed in (kg/cm^2).

The time required for the tablets to break-up into particles and pass through the mesh into the medium was noted and expressed in (min) as the disintegration time, using a disintegration test apparatus (Shivani scientific Ind., Mumbai, India).

Drug content assay

The drug content evaluation was performed according to USP specifications.[18] Powdered tablet equivalent to 250 mg of Paracetamol from samples obtained from each environmental condition at specific times, was accurately weighed and transferred into a 100 mL volumetric flask and appropriate dilution was made with phosphate buffer pH 7.4 and analyzed spectrophotometrically for drug content at λmax of 247 nm using a UV/VIS Spectrophotometer (Spectrum Lab 752s, England, UK).[25]

Statistical analysis

One-way ANOVA and student t-test statistical analysis were performed using GraphPad Prism 5, version 5.01 to compare the difference in data and a p-value < 0.05 was considered significant. Tukey's Post Hoc test was used to compare means of pairs to identify where the exact difference lies from the result obtained from the One-way ANOVA analysis.

Results and Discussion

Paracetamol tablets were exposed to different conditions most likely to be encountered during its shelf life. These conditions were adopted in this study to simulate the drug supply system of some pharmaceutical companies and freelance distributors whereby drugs are kept in various places including the trunk of cars for distribution. Obitte *et al*.[26] reported drug storage in cars. There is the possibility of drug remaining in this condition for over one year. The products that were kept out-door, directly under sunlight, heat and rain was to simulate the conditions of drug hawking and drug exhibition. In some areas in West Africa, drugs are being sold by hawking directly under the sun, heat and rain.[27,28] Also, some drug vendors exhibit drug products (just like other commodities such as cloths) directly under the sun in a bid to advertise and attract customers. The one kept in the living room and the kitchen is to simulate the conditions in which consumers after getting their prescription filled are likely to expose the drugs to. Many times, consumers keep drugs in the kitchen, living room or refrigerators. Jassim,[29] Tsiligianni *et al*.,[30] Pankajkumar *et al*.[31] reported high rate of inappropriate storage conditions which is a universal occurrence at homes. This study is therefore necessary to investigate the effect of these conditions on the pharmaceutical stability of paracetamol tablets.

Organoleptic properties of the tablets at 24 months revealed a smooth, white round, odouless, and uniformly-shaped tablets except for the brands kept out-door which had an off white colour appearance probably due to sunlight. Colour of the secondary packages was not affected except for the brands kept out-door due to the effect of sunlight and rain.

The thickness and weight of the three brands of paracetamol tablet as shown in Table 1 decreased generally with time across all environmental conditions which they were exposed to except P3 which had an increase in tablet thickness and weight for the tablets kept out-door and in the trunk. One way ANOVA indicated no significant difference in the thickness of P1 and P2 tablets across all conditions while P3 tablets kept out-door and in the trunk had a significant increase. There was significant difference in the tablet thickness of the three brands (P1, P2 and P3) when compared at same environmental condition in the order P1 > P3 > P2.

Statistical analysis indicated a significant difference in the weight of P1 and P3 across all the environmental conditions over time while there was no significant difference in P2 tablet weight at all environmental conditions. The weight of P1 tablets kept out-door and in the trunk significantly decreased over time while P3 tablets increased significantly. Tablets in the living room and kitchen had no significant effect on the weight of P1 and P3. There was significant difference in the tablet weight of the three brands (P1, P2 and P3) when compared at same environmental condition in the order P1 > P2 > P3.

The hardness of the three paracetamol tablet brands as presented in Table 2 increased while the friability decreased generally with time across the four environmental conditions which they were exposed to over time except P3 which had a decrease in tablet hardness and an increase in tablet friability for the tablets kept out-door and in the trunk. Statistical analysis showed a significant difference in the hardness of P1 and P3 tablets kept out-door and in the trunk while there was no significant difference for tablets kept in the living room and the kitchen. For P2, there was no significant difference in the hardness across all condition. For friability, there was no significant difference in P1 and P2 across all environmental condition, but there was significant difference

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Table 1: Effect of environmental condition on physical properties of paracetamol tablets.

		Thickness (mm)			Weight (g)		
EC	**TIME (months)**	**P1**	**P2**	**P3**	**P1**	**P2**	**P3**
	0	4.25 ± 0.07	3.69 ± 0.10	4.18 ± 0.29	0.572 ± 0.19	0.555 ± 0.04	0.521 ± 0.23
A	1	4.25 ± 0.21	3.70 ± 0.75	4.18 ± 0.63	0.574 ± 0.03	0.556 ± 0.35	0.520 ± 0.42
	3	4.26 ± 0.53	3.71 ± 0.48	4.17 ± 0.28	0.570 ± 0.32	0.556 ± 0.16	0.519 ± 0.86
	6	4.25 ± 0.26	3.72 ± 0.29	4.16 ± 0.59	0.572 ± 0.83	0.555 ± 0.44	0.519 ± 0.26
	9	4.23 ± 0.94	3.70 ± 0.57	4.17 ± 0.50	0.573 ± 0.73	0.557 ± 0.14	0.521 ± 0.12
	12	4.23 ± 1.53	3.69 ± 0.04	4.18 ± 0.04	0.571 ± 0.16	0.553 ± 0.28	0.520 ± 0.61
	18	4.21 ± 0.22	3.67 ± 0.43	4.16 ± 0.14	0.574 ± 0.72	0.551 ± 0.57	0.518 ± 0.03
	24	4.21 ± 0.36	3.65 ± 0.38	4.18 ± 0.10	0.571 ± 0.25	0.550 ± 0.02	0.518 ± 0.07
B	1	4.24 ± 0.26	3.71 ± 0.16	4.18 ± 0.18	0.573 ± 0.96	0.554 ± 0.36	0.521 ± 0.35
	3	4.25 ± 0.51	3.71 ± 0.24	4.17 ± 0.11	0.571 ± 0.83	0.553 ± 0.21	0.521 ± 0.26
	6	4.22 ± 0.72	3.69 ± 0.38	4.16 ± 0.32	0.572 ± 0.15	0.553 ± 0.22	0.519 ± 0.17
	9	4.22 ± 0.57	3.68 ± 0.27	4.17 ± 0.57	0.570 ± 0.32	0.552 ± 0.25	0.520 ± 0.74
	12	4.21 ± 0.27	3.68 ± 0.42	4.16 ± 0.04	0.571 ± 0.42	0.551 ± 0.43	0.518 ± 0.23
	18	4.18 ± 0.31	3.64 ± 0.23	4.12 ± 0.06	0.568 ± 0.31	0.547 ± 0.62	0.514 ± 0.51
	24	4.13 ± 0.27	3.60 ± 0.21	4.12 ± 0.25	0.564 ± 0.08	0.548 ± 0.10	0.512 ± 0.66
C	1	4.25 ± 0.22	3.71 ± 0.35	4.16 ± 0.48	0.571 ± 0.36	0.556 ± 0.47	0.522 ± 0.25
	3	4.23 ± 0.86	3.69 ± 0.23	4.20 ± 0.22	0.570 ± 0.40	0.553 ± 0.17	0.522 ± 0.23
	6	4.22 ± 0.41	3.69 ± 0.37	4.23 ± 0.16	0.569 ± 0.58	0.550 ± 0.93	0.524 ± 0.74
	9	4.20 ± 0.62	3.63 ± 0.55	4.28 ± 0.06	0.572 ± 0.53	0.549 ± 0.68	0.525 ± 0.06
	12	4.17 ± 0.96	3.65 ± 0.56	4.32 ± 0.71	0.568 ± 0.66	0.552 ± 0.15	0.528 ± 0.46
	18	4.10 ± 0.62	3.54 ± 0.07	4.40 ± 0.93	0.561 ± 0.71	0.543 ± 0.11	0.532 ± 0.14
	24	4.07 ± 0.14	3.51 ± 0.49	4.47 ± 0.41	0.559 ± 0.16	0.539 ± 0.02	0.539 ± 0.09
D	1	4.24 ± 0.52	3.70 ± 0.31	4.16 ± 0.97	0.570 ± 0.10	0.554 ± 1.22	0.520 ± 0.18
	3	4.23 ± 0.03	3.71 ± 0.21	4.19 ± 0.35	0.569 ± 0.12	0.552 ± 0.26	0.521 ± 0.15
	6	4.21 ± 0.31	3.69 ± 0.18	4.21 ± 0.19	0.568 ± 0.42	0.550 ± 0.12	0.523 ± 0.08
	9	4.18 ± 0.88	3.62 ± 0.52	4.25 ± 0.43	0.568 ± 0.15	0.551 ± 0.70	0.523 ± 0.26
	12	4.15 ± 0.53	3.62 ± 0.14	4.28 ± 0.38	0.562 ± 0.45	0.549 ± 0.12	0.526 ± 0.21
	18	4.11 ± 0.09	3.51 ± 0.22	4.33 ± 0.27	0.552 ± 0.17	0.542 ± 0.58	0.528 ± 0.18
	24	3.86 ± 0.14	3.50 ± 0.68	4.38 ± 0.21	0.547 ± 0.26	0.531 ± 0.41	0.534 ± 0.27

EC = Environmental condition, P1 = Paracetamol tablet brand 1, P2 = Paracetamol tablet brand 2, P3 = Paracetamol tablet brand 3, A = Living room, B = Kitchen, C = Out-door, D = Trunk.

in hardness of P3 tablets kept out-door and in the trunk while for tablets in the living room and kitchen, there was no significant difference. There was significant difference in the hardness and the friability of the three brands (P1, P2 and P3) when compared at same environmental condition. Increase in temperature is expected to speed up chemical reaction; according to Arrhenius equation, every degree rise in temperature increases chemical degradation rate by ten folds.[32] For tablets, this reaction will affect the process of physicochemical degradation of the tablets which is usually in a slow steady rate. The drastic temperature fluctuation of heat from sunlight and in the trunk may induce a thermal gradient between the materials on the surface of the tablets and the materials in the core of the tablets. The average temperature of the trunk ranged between 22^{o}C and 70^{o}C while the out-door environment ranged between 20^{o}C and 60^{o}C. This may result in the deterioration of tablet stability due to the formation of cracks which will lead to a loss of tablet mechanical strength as a result of increase in material porosity. This could be the reason for the reduction in the hardness of P3 tablets kept out-door and in the trunk.

Decrease in hardness and increase in friability of P3 kept out-door and in the trunk may be due to moisture absorption since it was packaged in a wide mouthed open jar container unlike P1 and P2 packaged in PVC blisters. Ahmad and Shaikh,[33] Monika *et al*.,[34] Anbarasan *et al*.[35] concluded that moisture could affect hardness and friability of tablets. This could also be the reason why the tablet weight and thickness of this brand (P3) kept out-door and in the trunk increased after 24 months. The increase in hardness and decrease in friability observed in P1 and P2 tablets kept out-door and in the trunk could be due to loss of moisture with increase in temperature.[36] This could also be the reason why the tablet weight and thickness of brands P1 and P2 reduced after 24 months. The disintegration time as presented in Table 3 increased generally over time across all the environmental conditions while drug content decreased. There was no significant difference in the disintegration time of P1, P2 and P3 tablets over time at all environmental conditions except P1 in the trunk. There was significant difference in disintegration time of the three brands when compared at same environmental condition in the order P3>P1>P2. The increase in disintegration time correlates with hardness for the three brands except P3 tablets kept out-door and in the trunk.

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Table 2: Effect of environmental condition on mechanical properties of paracetamol tablets.

		Hardness (kg/cm^2)			Friability (%)		
EC	**TIME (months)**	**P1**	**P2**	**P3**	**P1**	**P2**	**P3**
	0	6.67 ± 1.75	5.48 ± 0.72	12.18 ± 0.16	0.56 ± 0.32	2.32 ± 0.38	0.37 ± 0.04
A	1	6.66 ± 0.35	5.49 ± 0.51	12.10 ± 1.00	0.58 ± 0.39	2.35 ± 0.22	0.35 ± 0.93
	3	6.69 ± 0.81	5.53 ± 0.59	12.28 ± 0.47	0.57 ± 2.05	2.31 ± 0.23	0.31 ± 1.28
	6	6.62 ± 1.08	5.60 ± 0.82	12.42 ± 0.93	0.49 ± 0.06	2.31 ± 0.74	0.30 ± 0.32
	9	6.86 ± 0.23	5.62 ± 1.04	12.54 ± 0.86	0.42 ± 0.32	2.29 ± 0.15	0.28 ± 0.47
	12	7.12 ± 0.48	5.61 ± 2.22	12.61 ± 0.05	0.37 ± 1.11	2.30 ± 0.10	0.25 ± 2.11
	18	7.60 ± 1.00	5.79 ± 1.48	12.83 ± 0.79	0.25 ± 0.28	1.91 ± 0.17	0.16 ± 0.36
	24	7.85 ± 1.32	5.94 ± 1.32	12.96 ± 0.67	0.26 ± 1.76	1.77 ± 0.22	0.12 ± 0.62
B	1	6.78 ± 0.83	5.54 ± 0.06	12.00 ± 1.74	0.56 ± 0.48	2.32 ± 0.52	0.38 ± 0.57
	3	6.84 ± 1.95	5.59 ± 0.75	12.26 ± 0.46	0.55 ± 0.05	2.34 ± 0.66	0.34 ± 0.06
	6	6.90 ± 3.18	5.68 ± 3.00	12.53 ± 0.69	0.50 ± 0.25	2.30 ± 0.21	0.34 ± 0.03
	9	6.97 ± 0.76	5.72 ± 0.37	12.58 ± 0.72	0.41 ± 0.23	2.26 ± 0.03	0.30 ± 1.25
	12	7.11 ± 0.50	5.74 ± 0.53	12.32 ± 0.09	0.35 ± 0.82	2.17 ± 0.11	0.24 ± 0.13
	18	7.97 ± 0.11	5.85 ± 0.92	12.88 ± 0.39	0.28 ± 0.43	1.93 ± 0.18	0.11 ± 0.07
	24	8.88 ± 1.62	5.98 ± 0.37	12.92 ± 0.56	0.24 ± 0.16	1.61 ± 0.01	0.15 ± 0.24
C	1	6.69 ± 0.19	5.58 ± 0.13	12.27 ± 0.27	0.57 ± 0.50	2.35 ± 0.28	0.37 ± 0.27
	3	7.16 ± 0.76	5.65 ± 1.50	12.08 ± 0.88	0.54 ± 0.84	2.34 ± 1.09	0.40 ± 0.09
	6	7.51 ± 0.29	5.73 ± 0.82	11.91 ± 1.64	0.49 ± 0.32	2.26 ± 0.02	0.48 ± 0.25
	9	7.85 ± 0.37	5.81 ± 0.94	11.86 ± 1.95	0.45 ± 1.58	2.08 ± 0.74	0.52 ± 0.17
	12	8.10 ± 0.17	6.08 ± 0.54	11.52 ± 1.69	0.31 ± 0.34	1.95 ± 0.69	0.66 ± 0.04
	18	8.75 ± 1.61	6.29 ± 0.50	10.43 ± 1.77	0.26 ± 0.29	1.72 ± 0.41	0.78 ± 0.21
	24	8.96 ± 0.49	6.67 ± 0.02	9.28 ± 2.40	0.20 ± 0.64	1.17 ± 0.26	0.83 ± 0.37
D	1	7.01 ± 1.25	5.58 ± 0.84	12.22 ± 1.22	0.57 ± 0.16	2.30 ± 0.44	0.35 ± 0.14
	3	7.33 ± 0.61	5.69 ± 0.60	12.16 ± 1.05	0.52 ± 0.95	2.26 ± 0.18	0.41 ± 0.37
	6	7.57 ± 1.05	5.79 ± 0.28	11.97 ± 0.40	0.43 ± 0.22	2.12 ± 0.94	0.45 ± 0.26
	9	7.85 ± 0.85	5.85 ± 1.16	10.52 ± 1.70	0.36 ± 0.46	1.95 ± 0.08	0.47 ± 0.16
	12	8.17 ± 0.41	6.16 ± 0.45	11.35 ± 0.76	0.30 ± 0.32	1.81 ± 0.23	0.54 ± 0.29
	18	9.38 ± 1.00	6.51 ± 0.06	11.30 ± 0.61	0.21 ± 0.97	1.32 ± 0.16	0.62 ± 0.38
	24	9.89 ± 1.15	7.84 ± 0.55	10.28 ± 1.76	0.18 ± 0.41	1.20 ± 0.04	0.73 ± 0.52

The drug content of P1 and P3 (table 3) had no significant difference over time at all conditions while drug content of P2 kept out-door and in the trunk decreased significantly. Just as temperature fluctuation may lower mechanical strength, it may also lower the chemical resistance of materials thereby degrading tablet drug content.[37] This may also be the reason for the significantly degradation of the drug content of P2 tablets kept out-door for 24 months. This can be supported by the report of Mubengayi *et al*.,[38] who observed an abnormal drop of paracetamol content and release rate below official specification from the sixth month of storage. Generally, the drug content of tablets kept out-door and in the trunk were adversely affected after 24 months storage. This could be as a result of hydrolysis from the moisture in the tablets catalyzed by heat. Hydrolysis is the main degradative reaction of paracetamol.[39]

Generally, the stability of the three brands at all the environmental conditions was not remarkably affected at 24 months of storage except brand P3 that were kept out-door and in the trunk. Tsvetkova *et al*.,[40] Muti and Othman,[41] Raman *et al*.[42] observed that paracetamol tablets stability characteristics were not significantly affected under different storage conditions.

The various degree and extent of the stability issues observed between P1, P2 and P3 could likely be due to differences in formulation processes and excipients employed by different pharmaceutical companies. In this study, paracetamol is the common active pharmaceutical ingredient (API) in the three brands, thus the variable (different excipients) may be the cause of the stability problem.[43] Pure paracetamol powder on its own is stable to high temperature[44] thus; the adverse effect observed on stability could not have been due to paracetamol. It has been reported that stability of individual ingredient contributes greatly to the stability of the finished product.[1]

It is evident that the excipients used in the formulation of the three paracetamol brands are different since each brand had different baseline data and also reacted differently when exposed to the same environmental condition.

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Table 3: Effect of environmental condition on drug content and disintegration time of paracetamol tablets.

		Disintegration (mins)			Drug content (%)		
EC	**TIME (months)**	**P1**	**P2**	**P3**	**P1**	**P2**	**P3**
	0	6.35 ± 0.12	2.81 ± 0.73	4.12 ± 0.50	100.05	99.95	101.16
A	1	6.15 ± 0.07	2.80 ± 0.24	4.14 ± 0.16	99.94	99.95	101.12
	3	6.30 ± 0.61	3.06 ± 0.32	4.67 ± 0.78	99.85	99.91	99.08
	6	6.86 ± 0.36	3.62 ± 0.84	6.72 ± 0.02	99.77	99.90	98.95
	9	6.95 ± 0.24	3.27 ± 0.73	8.18 ± 0.63	99.32	99.92	97.01
	12	8.13 ± 0.09	4.13 ± 0.31	9.47 ± 0.17	99.21	99.81	96.78
	18	8.10 ± 1.29	4.86 ± 0.29	11.14 ± 0.46	99.17	99.70	95.92
	24	8.28 ± 0.73	5.42 ± 0.98	13.90 ± 0.44	99.03	99.53	95.48
B	1	6.32 ± 0.22	2.79 ± 0.09	4.11 ± 0.32	99.98	99.93	101.10
	3	6.39 ± 0.35	3.14 ± 0.80	4.83 ± 0.48	99.92	99.90	99.00
	6	6.63 ± 0.12	3.64 ± 0.01	6.95 ± 0.73	99.86	99.82	98.72
	9	8.06 ± 0.57	3.97 ± 0.16	8.48 ± 0.30	99.24	99.74	96.96
	12	8.22 ± 0.34	4.44 ± 0.24	9.90 ± 0.25	99.15	99.61	96.03
	18	8.41 ± 0.87	4.81 ± 0.21	10.94 ± 0.92	99.09	99.44	95.46
	24	9.86 ± 0.44	5.96 ± 0.24	13.21 ± 0.44	99. 01	98.37	95.12
C	1	6.36 ± 0.02	2.85 ± 0.63	4.22 ± 0.11	100.02	99.96	99.93
	3	6.48 ± 0.05	3.72 ± 0.71	5.35 ± 0.03	99.92	99.60	98.60
	6	7.94 ± 0.18	3.88 ± 0.40	8.04 ± 0.73	99.78	99.51	97.31
	9	8.27 ± 0.06	4.16 ± 0.31	10.85 ± 0.93	99.61	99.42	96.06
	12	9.83 ± 1.75	5.25 ± 1.08	12.86 ± 0.10	99.50	99.11	95.12
	18	10.15 ± 0.47	6.73 ± 0.27	14.23 ± 0.62	99.17	98.03	93.06
	24	12.46 ± 0.65	8.29 ± 0.95	16.96 ± 0.15	98.01	97.49	91.82
D	1	6.84 ± 0.11	2.82 ± 0.58	4.10 ± 0.02	99.82	99.85	100.36
	3	8.44 ± 0.05	3.91 ± 0.80	4.93 ± 0.09	99.70	99.51	98.93
	6	9.82 ± 0.36	4.37 ± 0.27	7.25 ± 0.25	99.36	99.12	97.28
	9	10.69 ± 0.58	4.96 ± 0.32	9.73 ± 0.93	99.18	98.92	96.15
	12	12.53 ± 0.25	6.76 ± 0.39	11.30 ± 0.36	98.03	98.01	95.04
	18	15.15 ± 0.47	8.94 ± 0.22	13.62 ± 0.10	96.12	96.15	94.39
	24	18.12 ± 2.07	10.66 ± 1.53	14.96 ± 0.15	95.21	95.05	93.08

Conclusion

The stability of paracetamol tablet formulations depended greatly on the primary packaging and conditions of storage in terms of heat and moisture. The extent of drug degradation was minimal in products packaged in PVC blisters compared to those loosely packaged in a wide mouthed open plastic jar. The pharmaceutical stability of the three brands stored in the living room and in the kitchen was not adversely affected while the brands that were kept out-door and in the car trunk, especially P3 had their stability greatly affected. The choice of excipients that could withstand adverse conditions would enhance stability of paracetamol tablet formulations.

Conflict of interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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