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EFFECT ON TEMPERATURE ON PHYSICOCHEMICAL PROPERTIES OF PARACETAMOL SUSPENSION PACKAGED IN PLASTIC/GLASS CONTAINERS

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Abstract

Study of the effect of various temperatures (25°C, 40°C, 50°C) on the physicochemical properties including potency of paracetamol suspension in different plastic bottles (polyethylene opaque/ transparent, polyvinyl chloride) and glass bottle has been made over a period of 2 months. different storage temperatures (25°C,40°C,50°C,) freshly prepared standard suspension plus five modified formulation packaged in plastic /glass container were stored for 2 months and their physical properties plus pH; and viscosity were determined by routine test methods and potency were determined using H.P.L.C method. To exclude the effect of temperature fluctuation on different excipients these five formulation of paracetamol having different composition were examined under the same standards.The results show a marked decrease on these parameters under different temperatures. Glass has been observed as the most resistant packaging materiel to temperature difference whereas. P.E. (transparent) has been observed as most labile packaging material to temperature difference P.E (opaque) showed better results than PE. (transparent), whereas, P.V.C. shows better results than P.E (opaque).

The order of deviation was: Glass >. P .V. C > P.E (transparent)

Key Words: **temperature effect, paracetamol/suspension in plastic/glass containers,**

Introduction

The stability of pharmaceutical products are usually affected by temperature fluctuations on different packaging materials during storage in shelf life. variation in temperature causes drug-container interaction and as a result the composition of the product is affected. Thus a relation between container and content could be vital for the retention of product quality. The common practices of storing drugs is plastic container is of particular interest due to their relatively low cost, nonfragile type and availability in large variety. A scientific approach to the problem of durg-container interaction and development of sensitive analytical and toxicological test methods are needed for evaluating any hazards associated with changes in the properties of packaged medicaments.

The present study has been made to assess the effect of temperature on the stability of paracetamol suspension packaged in Plastic Glas Bottles.

In this study a paracetamol suspension was prepared according to standard method and five other formulations were prepared in laboratory having variable composition (Table:1).

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Table No.1
Formulation of paracetamol suspension

Formulation No.	Paracetamol	Gum Acacia	No CMC	Sugar	Sodium Saccahrin	Glycerine	Sodium benzoate	Methyle Paraben	Prioyk Paraben	PG	Alcohol	Pink Colour	
Standard Formulation	+	+	+	+	+	+	+	+	+	+	+	+	-
Formulation No.1	+	+	+	+	+	+	+	+	+	+	+	+	-
Formulation No.2	+	+	++	+	+	+	+	+	+	+	+	+	-
Formulation No.3	+	+	+	+	+	+	+	+	+	-	+	+	-
Formulation No.4	+	+	+	+	+	+	+	-	-	+	+	+	-
Formulation No.5	+	+	+	+	+	+	-	-	-	+	+	+	-

Na CMC Sodium Corboxymethlcellulose PG Propylene Glycol

(-) Absent
(+) Present (++) Increased Cone"

The formulations were made as:
Standard paracetamol suspension
Paracetamol suspension without Gum acacia.
Paracetamol suspension with increased Conc" of Na CMC.

Paracetamol suspension without sodium benzoate and alcohol.
Paracetamol suspension without Methyle & Poropyleporaban
Paracetamol suspension without all preservatives.

These preparations were stored at different temperatures: 25C°, 40C°, 50C° for 2 months in plastic bottles of different types as Polyethylene opaque (PEO) Polyethylene Transparent (PET) and Polyvinyl Chloride (PVC) and in glass bottles. The suspension were analysed as freshly prepared, after one month & after 2 months, to see the changes in colour, odour, taste, pH, viscosity; specific gravity by routine test methods and potency was determined by HPLC method according to USP 1995.

Materials and methods

a. Chemicals

Acetaminophen USP, Methanol, Distilled Water
All chemicals and reagents were purchased from E-Merck.

b. Methods

According to USP 1995.

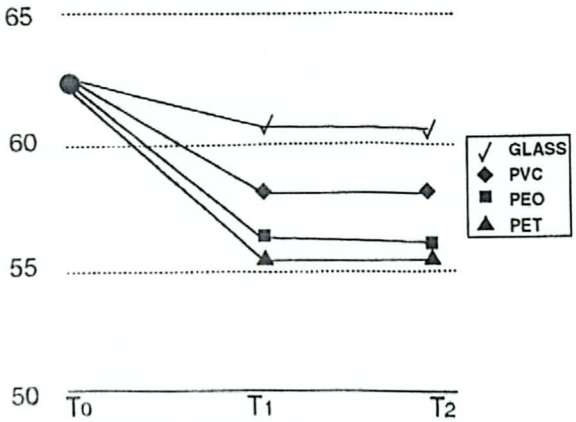
Results and discussion

Pharmaceutical products packaged in different containers are usually affected by temperature variations and during shelf life interaction between product and container, the change in pH of the product is accelerated by leaking of alkaline or acidic materials from the container or deterioration caused by heat exposure or other environmental conditions. The change in pH values during storage of drugs therefore leads to toxicity, potency loss; disintegration and formation of new compounds and certain redox and hydrolysis type reactions. Thus the quality of drug is affected due to loss of potency and the choice of unsuitable containers made either of glass or plastic.

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Effect of temperature on pH of suspension with increased storage times:

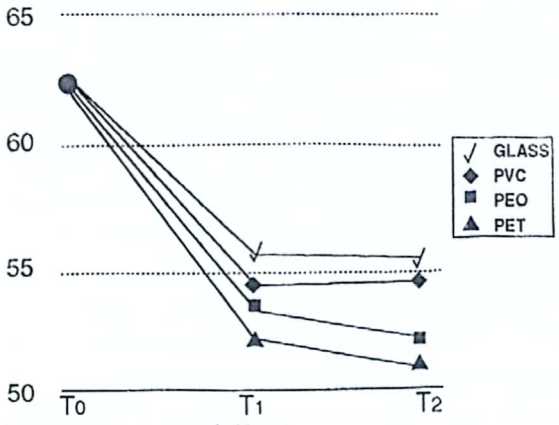
The effect of temperature on pH of suspension in Glass and different plastic bottles: PVC; PEO; and PET at different temperatures and at different storage time periods was observed (table No. 2,3 & 4 and graphs 1,2 & 3 respectively). While the effect of temperature on pH of suspension of five different compositions at different storage time periods is presented in table NO. 5. and graph 4.



Graph No: 1

Table No.2
Change in pH of paracetamol Suspension stored at 25°C

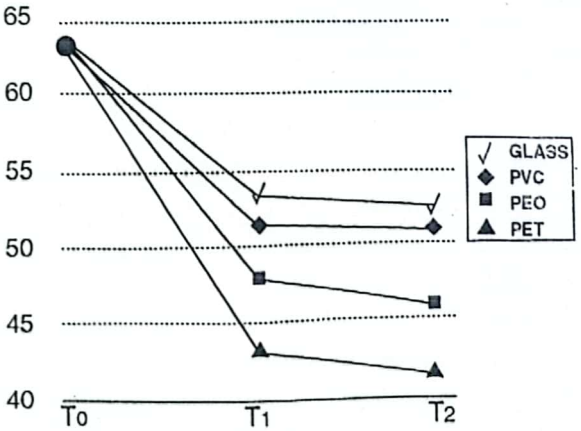
S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	6.25	6.15	6.12
2	PVC	6.25	5.85	5.82
3	PED	6.25	5.68	5.65
4	PET	6.25	5.62	5.6



Graph No: 2

Table No:3
Change in pH of paracetamol Suspension stored at 40°C

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	6.25	5.57	6.55
2	PVC	6.25	5.44	5.43
3	PED	6.25	5.35	5.28
4	PET	6.25	5.26	5.15



Graph No: 3

Table No:4
Change in pH of paracetamol Suspension stored at 50°C

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	6.25	5.28	5.25
2	PVC	6.25	5.16	5.12
3	PED	6.25	4.82	4.6
4	PET	6.25	4.21	4.12

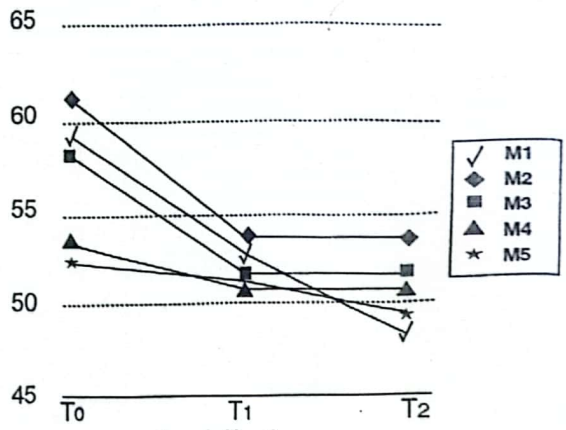
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The results in table 2,3,4 and 5 showed a gradual decrease in pH of suspension with increase in temperature and storage time. The change in pH during storage may be due to release of small quantities of chemical agents to the solvent system (3,7,10). Change in pH can also cause a loss of potency due to its effect on activity of preservative (2) the decrease in pH may also be due to interaction of any excipient for instance the mucilage of gum acacia turns acidic on storage due to enzyme activity and contains an oxidase enzyme may cause deterioration of active agent susceptible to oxidation.

Effect of temperature on viscosity of suspension with increased storage time:

Effect of temperature with increased storage time on viscosity of suspension in Glass and different plastic bottles: (PVC); PEO and PET) at different temperatures and at different storage time periods is listed and plotted in tables of No. 6,7,8 and graphs 5,6,7 respectively. While effect of temperature on five different compositions of paracetamol suspension at different storage time periods is presented in table 9 and graph 8. The results show gradual decrease in viscosity which is more pronounced in plastic bottles than glass.

This change in viscosity of suspension stored in various types of different containers at different temperature may be due to viscosity stability of methyl cellulose at different pH and temperature. Since change in temperature causes change in pH which inturn causes change in viscosity. Accordion to Huikari Ansa (1989[4], a continuous decrease in viscosity with storage temperature usually takes place due to a deploymerization of carboxymethyl cellulose. According to MR Billany [3] decrease in viscosity is due to decrease in pH the caused by presence of Gumaccacia which becomes acidic on storage. According to Shangraw R.F & Walking W.d)[8], an interaction of acetaminophen and sodium carboxymethyl celluslose causes a marked decrease in viscosity of suspension. Another cause of change in viscosity is the decomposition of active ingredients due to interaction of excipients and active ingredients or interaction of product-container or due to the nature of thickening agent and its compatibility to other excipents.

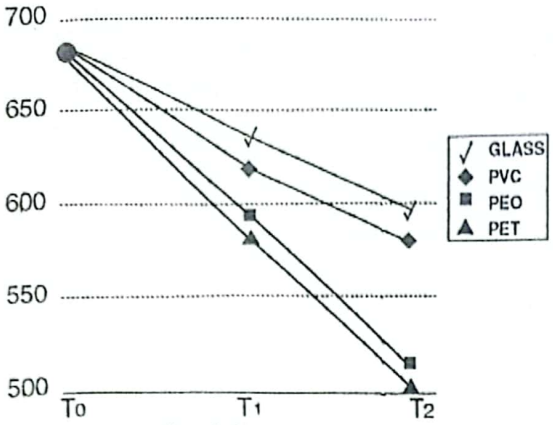


Graph No: 4

Table No:5
Change in pH of Modified formulation of Paracetamol suspension

S.No	Nme of Formulation	Storage Time iMonth		
		T_0	T_1	T_2
1	M1	5.92	6.39	4.95
2	M2	6.07	5.35	5.27
3	M3	5.88	5.3	5.2
4	M4	5.45	5.22	5.1
5	M5	5.4	5.27	5.01

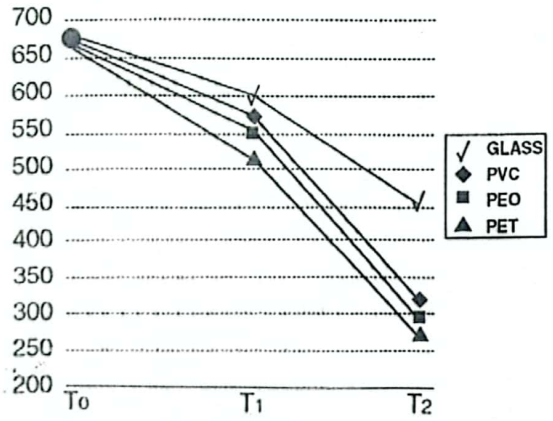
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Graph No: 5

Table No:6
Change in Viscosiaty of paracetakmol Suspension stored at 25°C

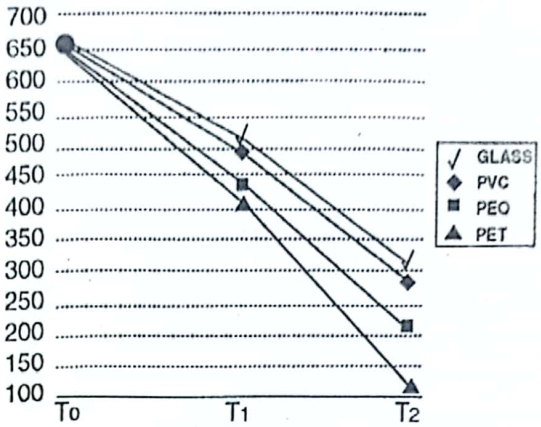
S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	680	640	600
2	PVC	680	624	580
3	PED	680	596	510
4	PET	680	584	500



Graph No: 6

Table No:7
Change inViscosity of paracetamol Suspension stored at 40°C

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	6.08	610	460
2	PVC	6.80	585	300
3	PED	6.80	560	290
4	PET	6.80	510	280



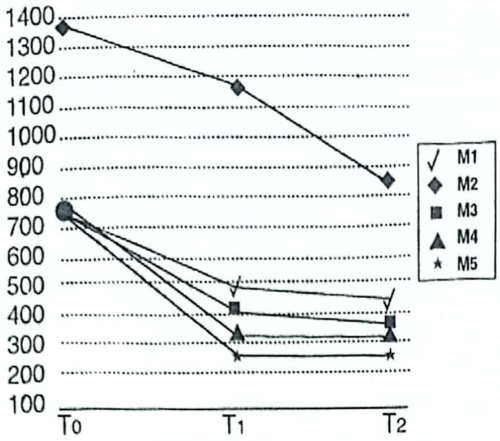
Graph No: 7

Table No:8
Change in Viscosity of paracetamol Suspension stored at 50°C

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	680	500	300
2	PVC	680	490	275
3	PED	680	425	210
4	PET	680	410	100

The change in viscosity during storage changes the appearance of the product causes improper dosage and loss of quality of product.

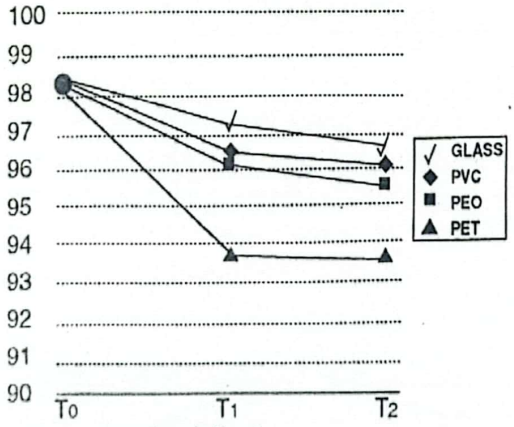
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Graph No: 8

Table No:9
Change in Viscosity of Modified formulation of paracetamol suspension

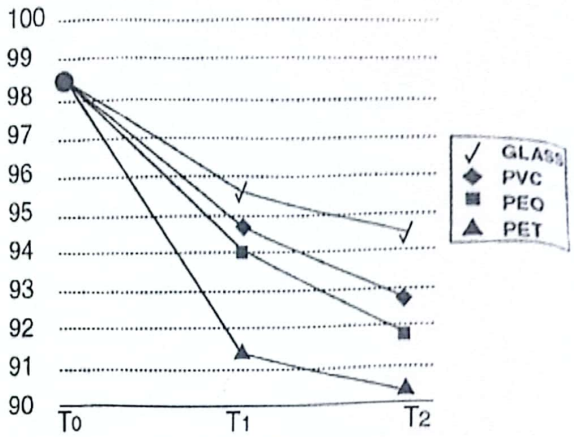
S.No	Nme of Formulation	Storage Time in Month		
		T_0	T_1	T_2
1	M1	712	480	444
2	M2	1356	1172	760
3	M3	748	388	348
4	M4	756	324	300
5	M5	728	312	277



Graph No: 9

Table No:10
Change in Assay of paracetamol Suspension stored at 25°C

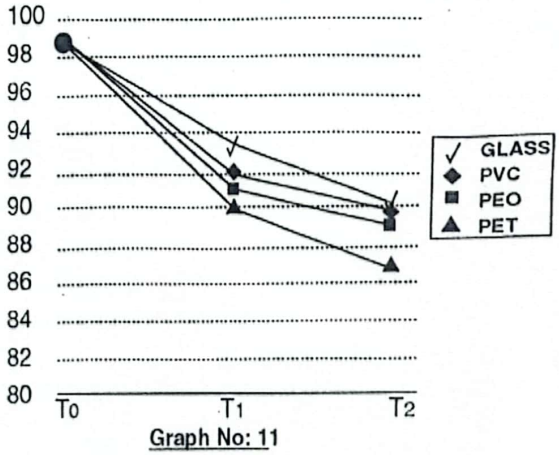
S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	98.25	97.23	96.79
2	PVC	98.25	96.25	96.27
3	PED	98.25	96.45	95.6
4	PET	98.25	93.75	93.6



Graph No: 10

Table No:11
Change in Assay of paracetamol Suspension stored at 40°C .

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	98.25	95.42	94.55
2	PVC	98.25	94.77	92.78
3	PED	98.25	93.98	91.58
4	PET	98.25	91.38	90.58



Graph No: 11

Table No:12
Change in Assay of paracetamol Suspension stored at 50°C

S.No	Type of cotainers	Storage Time in Month		
		T_0	T_1	T_2
1	GLASS	98.25	93.32	88.99
2	PVC	98.25	91.15	88.82
3	PED	98.25	90.14	88.76
4	PET	98.25	89.94	87.23

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Effect of temperature on potency of suspension with increased storage time:

The effect of packaging material on the potency of product is due to physico-chemical factors or due to any interaction between product and container. These interactions are usually accelerated by change in temp. (Shotten[9]).

The results show a loss in potency by increase in temp. during shelf life. Different packaging materials: glass; plastics (PVC; PEO; PET) show variable results as in tables No (10; 11; 12) and

graphs 9,10,11 respectively. While the potency variation of five different compositions with respect to storage time are given in table No. 13 and graph 12. The results showed a dercease in potency of suspension in all containers with increasing storage time at elevated temp. the extent of decrease in potency in glass container is less than in plastic containers. Among five different compositions the formulation No. 4,5 showed a greater decrease in potency, this may be due to complete absences of preservatives.

Beside pH, viscosity and potency; the specific gravity and physical appearance (colour, odour) of standard as well as of sample formulations of paracetamol suspension were noted and it was found that physical appearance (colour, odour) changes due to increased temperature and storage time. These results clearly show that the Glass container is far superior to plastic.

According to Autian 1964[1] Plastic is not as safe as originally thought. It does not mean that plastic should be banned or eliminated from medical practice, rather a method should be sought which should ensure that a particular plastic or device will be safe for intended use, standards must be created for medicinal use of plastics as well as fine plastic devices.

Since Glass is inconvenient because of its transportation cost, and fragile nature plastic has therefore taken the top place in the packaging industry. But the disadvantages of plastic are quite enough to deteriorate the product [5,6]. Therefore evaluation of plastic material and introduction of blended plastic seems to solve this problem. A rational approach to the packaging containers should be adopted to over come all sorts of substanderdisation of the packaging product.s.

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