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FORMULATION AND EVALUATION OF BENZOYL METRONIDAZOLE SUSPENSION

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ABSTRACT

Two formulae of benzoyl metronidazole suspension were prepared. One consisted of Tween 40 (0.2%), sodium carboxymethyl cellulose (1%), and potassium dihydrogen phosphate (0.002%) [formula No. 1] and sodium chloride (.005%) instead of potassium dihydrogen phosphate [formula No. 2]. The formulated suspensions, were found to be superior than the commercial one. The sediment was one layer compared to two layers sediment of the commercial product. The supernatants were clear and the suspensions were easily redispersed. The percent drug dissoluted was higher than that of the commercial product. The prepared suspensions showed physical and chemical stability even after 12 months of aging.

INTRODUCTION

Metronidazole benzoyl ester demonstrated certain instability problems when prepared in suspensions[1]. It was reported that preliminary tests showed that benzoyl metronidazole underwent some colour change on keeping in phosphate buffer at pH7[2]. So, the stability of benzoyl metronidazole was studied[2], in different suspension stabilizers and different dispersion media of different pH[2]. Combination of kaolin and citric acid-phosphate buffer at pH 5.0 has been found to be highly recommended regarding elegancy, stability and maximum drug release (97.3%)[2].

Metronidazole benzoate shows physical stability problems when stored in the cold, in that a marked crystal growth may occur[1]. This increase of the particle size has recently been shown to be due to phase transition of the anhydrous form of the metronidazole ester[1]. By inclusion complexation of metronidazole ester with B-cyclodextrin[3], this phase transition in aqueous suspension was inhibited. Beside increasing the physical stability of metronidazole benzoate suspensions, the complexation with B-cyclodextrin protected the drug against photochemical degradation and decreased the rate of hydrolysis.

As elicited from the previous paper[4], the commercial products of benzoyl metronidazole suspension, exhibited inter-and intrabatch variations. Moreover the number of the large particles increased by aging[4]. So, the aim of the present study is to formulate and evaluate benzoyl metronidazole suspension.

EXPERIMENTAL

Materials :

Bezoyl metronidazole powder, supplied by Alexandria Co., Egypt. All chemicals and reagents were either of analytical or pharmaceutical grade and were used without further purification.

1-Formulation of Suspensions:

A- Effect of Surfactants on the Wettability of Benzoyl Metronidazole Powder : The apparatus used consists of an open ended glass tube, the tube was plugged at its lower end with a wrapped filter strip (2 cm height) and packed with benzoyl metronidazole powder with particle size 90-63 um to a constant height of 5 cm. The packing was not too loose to produce heterogeneous porosities through the powder column. The tubes were dipped to one centimeter depth in the solution of the tested surfactant. The extent of penetration of the liquid through the column was measured in centimeters.

B- Thickening Agents : The thickening agents were dissolved in water, the drug was levigated with the wetting agent, then the solution of the thickening agent was added and the sedimentation volume was determined.

C- Flocculating Agents : The flocculating agents were dissolved in water, the drug was levigated with wetting agent, then the solutions of the flocculating agent and the thickening agent were added. The drug was dispersed thoroughly and was transferred into stoppered graduated cylinder, and the sedimenta-

tion volume was determined. The degree of flocculation was calculated using the following equation[5].

$$B = \frac{Vu/Vo}{V_\infty/Vo} = Vu/V_\infty$$

Ultimate sediment volume of Flocculated Suspension.

B= ----------

Ultimate sediment volume of deflocculated suspension

Preparation of Suspensions :

Benzoyl metronidazole powder, 200 mg/5ml equivalent to 125 mg metronidazole was levigated with the chosen surfactant solution in a mortar, the flocculating agent and the equeous dispersion of the suspending agent were added with thorough trituration. The suspension was transferred to 25-ml glass stoppered measuring cylinder. The volume of the suspension was completed with distilled water to make 25 ml. Preservatives viz., methylparaben (0.15%) and propyl paraben (0.2%) were added to the formulated suspensions to prevent the growth of microorganisms. The pH of suspension were within the range of 5.6-5.8. The cylinders were stoppered, shaken and stored in an oven at 30°C. The prepared suspensions were evaluated at different time intervals using the preceding cited parameters for their stability[4], viz., clarity of supernatant, redispersibility, sedmintation volume, drug content, particle length, dissolution behaviour and discoloration.

Thin-layer chromatography (TLC) was also carried out for determination of the stability of benzoyl metronidazole suspension. The system consisted of chloroform, acetone and glaial acetic acid at ratio 85 : 10 : 7.5 respectively. The system was proved to be capable of separating the degraded product. Ultraviolet lamp or iodine vapour was used for the detection of metronidazole spots.

RESULTS AND DISCUSSION

1-Formulation of Benzoyl Metronidazole Suspension.

a-Particle Size : The dissolution rate studies were carried out on different particle sizes of benzoyl metronidazole powder,differing from more than 90, 90-63 and less than 63 um (Fig.1) It was observed that the particles > 90 um gave the highest dissolution rate but the particle size range of 90-63 Um was chosen for further studies for its abundance.

b-Non-Ionic Surfactants : The wettability of benzoyl metronidazole powder was measured in absence and presence of solutions of Tween 20,40,60 and 80 (Table 1). The rate of penetration of water through the drug column was relatively slow, indicating partial hydrophobicity of benzoyl metronidazole powder. The chosen surfactant solutions instead of water were found to wet the drug powder to varying degrees, depending mainly on the chemical structure of each surfactant and its concentration. The surfactants were found to be more efficient as wetting agents as their concentration increased up to 0.2%. Tween 40 at concentration 0.2% was the best non-ionic wetting agent compared with Tween 20, Tween 60 and 80 after 20 minutes.

c-Thickening Agents :

1-Natural Thickening Agents :

For the naturally occuring thickening agents; gum acacia, gum tragacanth and agar were used as stabilizers for benzoyl metronidazole suspension. Table 2 shows that : gum acacia, when used in 8% concentration yielded suspension exhibiting no phase separation after 15 days, while drug suspension stabilized by 4% of acacia showed relatively low sedimentation volume, clear supernatant and ease of redispersion.

On using gum acacia in 6% concentration the sedimentation volume of suspension lies in between that stabilized by 4 and 8% but not easily redispersed. All the produced suspensions formulated with gum acacia exhibited pinkish discoloration after few days from preparation which intensified after 15 days. This discoloration increased with increasing the concentration of gum acacia. It could be attributed to the presence of peroxidase enzyme in acacia which could catalyze drug decomposition[6]. On the other hand, suspensions stabilized by gum tragacanth in concentrations of 0.2,0.4 and 0.6% showed relatively low sedimentation volume when fresh. The sedimentation volume slightly increased on storage. The increase in sedimentation volume, accompanying aging of suspension, could be due to the swelling character of bassorin fraction of tragacanth on standing[7]. Suspension stabilized by agar agar in concentrations 0.5,0.75 and 1% showed no phase separation at the highest concentration (1%) up to 10 days. At the lowest concentration (0.5%) the sedimentation volume was small with turbid supernatant which was dispersed after 3 to 4 times inversions.

2-Water-soluble Cellulose Derivatives:

Different concentrations of methocel E_{15} and sodium carboxymethylcellulose were used to stabilize benzoyl metronidazole suspension. From Table 3 it was observed that : The drug suspension stabilized by 0.5, 1 and 2% methocel exhibited very low sedimentation volume with clear supernatant and easily redispersed. On storage for 15 days the sedimentation volume of this suspension decreased. Sodium carboxymethylcellulose seemed to be the best stabilizer. At high concentration (2%) no phase separation was noticed after 15 days. One percent sodium carboxymethylcellulose gave high sedimentation volume, while the lower concentration 0.5 percent showed high sedimentation volume when fresh but on standing this parameter was decreased. All the suspensions prepared by 0.5 and 1% sodium carboxymethylcellulose showed clear supernatant and easily redispersed.

3-Finely-Dispersed Stabilizers :

Aerosil and kaolin were used in different concentrations for the stabilization of benzoyl metronidazole suspension. Table 4 showed that the suspensions stabilized by 1 and 2% aerosil showed low sedimentation volume which increased gradually on storage. On using 4% concentration of aerosil high sedimentation volume was observed with turbid supernatant. On standing this suspension became viscous and not easily redispersed. Increase the sedimentation volume of drug suspension stabilized by aerosil night

be due to the swelling characterizing the earth silicates. This finding is in agreement with that mentioned about the hydration of clays and gums[8].

The drug suspension stabilized by kaolin showed high sedimentation volume when fresh and this parameter gradually decreased on storage with formation of turbid supernatant and the suspension was easily redispersed.

On conclusion sodium carboxymethylcellulose in 1% concentration was chosen as the suitable stabilizer for formulation of benzoyl metronidazole powder.

d-Electrolytes : Electrolytes such as potassium dihydrogen phosphate, sodium chloride, aluminium chloride and calcium chloride were used to achieve flocculation of benzoyl metronidazole suspension stabilized by sodium carboxymethylcellulose (Table 5 & 6). Table 5 illustrates that potassium dihydrogen phosphate and sodium chloride at low concentrations (0.001-0.4% w/v) yield suspensions exhibiting both high sedimentation volume and high degree of flocculation with clear supernatant. At high concentration (1 and 2%) the sedimentation volume and the degree of flocculation were low. This may be due to the loss of viscosity of benzoyl metronidazole suspension stabilized with sodium carboxymethylcellulose. This loss of viscosity might be due to the salting out effect of the high concentrations of sodium chloride. It was reported that high concentration of electrolytes can lead to salting out of cellulose stabilizers[6].

Aluminium chloride and calcium chlroide (Table 6) at low concentrations 0.005 and 0.001% respectively showed high sedimentation volume and high degree of flocculation. Increase of the concentration lead to decrease in both parameters.

It could be concluded that potassium dihydrogen phosphate and sodium chloride in low concentrations were the best flocculating agents for preparing benzoyl metronidazole suspension. From Table 5 it was observed that 0.002 and 0.005% of potassium dihydrogen phosphate and sodium chloride respectively were the optimum concentrations used for the formulation of suspension which gave high sedimentation volume and high degree of flocculation. Moreover the supernatants were clear and easily redispersed.

From the above discussion Tween 40 (0.2 %) as the best wetting agent, potassium dihydrogen phosphate (0.002%) and sodium chloride (0.005%) as flocculating agent as well as sodium carboxymethylcellulose (1%) as the best thickening agent were chosen to formulate benzoyl metronidazole suspensions. Two formulae were prepared one contains potassium dihydrogen phosphate (formula No. 1) and the other contains sodium chloride as flocculating agents (formula No. 2). Preservatives viz; methylparaben (0.15%) and propylparaben (0.02%) were added to the formulated suspensions to prevent the growth of micro-organisms.

On using Macillivan's and phosphate buffer for formulation of suspensions at different pH values it was observed that sodium carboxymethylcellulose lost its viscosity at different pH values. Hence distilled water was used instead for preparation of the suspensions. The pH of suspensions was measured and found to be within the range of 5.6-5.8.

Evaluation of the Formulated Suspensions :

The formulated suspensions were evaluated according to the aforementioned parameters. Table 7 shows the calculated sedimentation volumes of the formulated suspensions where the sedimentation volume was high after the first two days of preparation and then decreased slightly by time. The supernatant was clear and the sediment was easily redispersed when fresh and after aging for 60 days while the commercial suspensions require 4-5 times of inversions to achieve redispersibility after aging for one day only[4].

Concerning the drug content there were no significant differences between bottles of the same formula. The percent benzoyl metronidazole recovered was within the range of 96.9-98.3%. This value was in agreement with that obtained from the previously formulated suspension with kaolin at pH5[2].

Determination of particle length revealed that there were no significant differences between the two formulae. (Fig. 2).
It was worthy to note that the sediment forming one layer only in contrast to that with commercial product which forms two layers[4].

Determination of the dissolution behaviour of the formulated suspensions showed that the maximum percent dissolved of benzoyl metronidazole after 5 minutes was 64.5 and 65% for formulae 1 and 2 respectively (Fig. 3). After 30 minutes it was observed that the maximum amount dissolved was 89 and 86% from formulae 1 and 2 respectively. After two hours the amount dissolved from the two formulae seemed to be equal (98.5%) where these values were higher than that, of commercial suspension[4]. There was no significant differences ($P \leq 0.05$) in the amount dissolved and K value between the four bottles of each formula (Table 8). Furthermore, the difference was insignificant ($P \leq 0.05$) between the two formulae.

The suspensions were reevaluated after 2,4,6,8 and 12 months for the drug content, particle length (Fig. 2) and the dissolution behaviour (compare Table 8 by Table 9). No detectable differences in these parameters between fresh and stored samples were recorded. These data were confirmed by TLC[4], which showed that benzoyl metronidazole was stable after 12 months of formulation into suspensions. Also, no detectable change in pH and the colour of suspensions was observed.

Table 1 : Effect of Different Wetting Agents on the Wettability of Benzoyl Metronidazole Powder.

Surfactant	Surfactant Concentration % w/v	Mean values of penetration (ml) of surfactant solution after (min) 5	10	15	20	30	40	50	60
Tween 20	0.05	--	--	--	--	--	--	--	--
	0.1	--	--	--	--	--	--	--	--
	0.2	2.5	2.7	3.0	3.4	3.6	3.9	4.0	4.2
Tween 40	0.05	--	--	1.8	2.0	2.3	2.5	2.7	3.0
	0.1	--	--	2.0	2.6	2.7	2.9	3.1	3.2
	0.2	3.0	4.0	4.8	5.0	5.0	5.0	5.0	5.0
Tween 60	0.05	2.0	2.6	2.8	2.8	2.9	3.2	3.6	3.9
	0.1	2.3	3.0	3.1	3.2	3.8	4.0	4.2	4.6
	0.2	2.6	3.2	3.4	3.7	4.0	4.2	4.6	5.0
Tween 80	0.05	--	--	--	--	2.0	2.2	2.3	2.4
	0.1	2.6	3.1	3.5	4.2	4.3	4.5	4.6	4.6
	0.2	3.2	3.7	4.0	4.2	4.7	4.8	4.8	4.8

Table 2 : Effect of Natural Stabilizers on the Physical Stability of Benzoyl Metronidazole Deflocculated Suspension.

Stabilizer	Concentration % w/v	Sedimentation Volume After Specified Time Intervals (days) 1	2	4	6	8	10	12	15	Number of Inversions after 15 days	Clarity of supernatant
Agar Agar	0.5	0.6	0.6	0.55	0.5	0.5	0.45	0.4	0.35	3	Turbid
	0.75	0.75	0.7	0.7	0.7	0.68	0.65	0.65	0.6	4	,,
	1	1	1	1	1	1	0.99	0.98	0.98	-	Thick and no phase Separation
Gum Acacia	4	0.6	0.55	0.5	0.45	0.4	0.35	0.3	0.3	3	Clear supernatant and easily redis-persed
	6	0.9	0.85	0.8	0.8	0.78	0.75	0.7	0.69	5	Clear supernatant and not easily redispersed
	8	1	1	1	1	1	1	1	1	-	No phase separation
Gum Tragacanth	0.2	0.05	0.1	0.13	0.15	0.16	0.17	0.17	0.17	1	Clear supernatant
	0.4	0.13	0.14	0.18	0.2	0.22	0.23	0.24	0.24	1	and eaSlly redis-persed
	0.6	0.2	0.3	0.31	0.35	0.36	0.37	0.37	0.38	1	

Table 3 : Effect of Water Soluble Cellulose Derivatives on the Physical Stability of Benzoyl Metronidazole Deflocculated Suspension.

Stabilizer	Concentration % w/v	Sedimentation Volume After Specified Time Intervals (days) 1	2	4	6	8	10	12	15	Number of inversion after 15 days	Clarity of Supernatant
Methocel E_{15}	0.5	0.3	0.3	0.28	0.25	0.25	0.22	0.2	0.15	1	Clear Supernatant
	1	0.4	0.39	0.35	0.35	0.33	0.3	0.28	0.25	1	and easily
	2	0.45	0.43	0.4	0.38	0.35	0.35	0.3	0.3	1	redispersed
Sodium Carboxy methyl Cellulose	0.5	1	1	1	0.98	0.95	0.88	0.86	0.7	1	Clear supernatant
	1	1	1	1	1	1	0.99	0.98	0.95	2	and easily redispersed
	2	1	1	1	1	1	1	1	1	-	No phase separation

Table 4 : Effect of Finely Dispersed Stabilizers on the Physical Stability of Benzoyl Metronidazole Deflocculated Suspension.

Stabilizer	Concentration % w/v	Sedimentation Volume After Specifled Time Intervals (days) 1	2	4	6	8	10	12	15	Number of inversion after 15 days	Clarity of Supernatant
Aerosil	1	0.23	0.25	0.28	0.3	0.32	0.35	0.35	0.35	3	Turbid supernatant and
	2	0.38	0.4	0.45	0.5	0.55	0.57	0.55	0.55	3	easily redispersed
(hydrophilic)	4	0.8	0.82	0.85	0.88	0.9	0.9	0.9	0.85	7	Turbid supernatant and not easily redispersed.
Light Kaolin	1	0.9	0.7	0.6	0.55	0.5	0.35	0.22	0.2	-	Turbid supernatant and
	2	0.95	0.8	0.75	0.65	0.6	0.5	0.4	0.35	-	easily redispersed
	4	1	0.95	0.9	0.8	0.78	0.69	0.65	0.55	-	

Table 5 : Effect of Potassium Dihydrogen Phosphate and Sodium Chloride as Flocculating Agents on Benzoyl Metronidazole Suspension Stabilized with Sodium Carboxymethylcellulose.

Electrolyte	Concentration % w/v	Sedimentation Volume After Time Intervals(days) 2	8	15	30	45	60	Number of inversions after(days): 2	15	60	Degree of Flocculation after 15 days	Clarity of supernatant
	0.000	0.86	0.74	0.70	0.68	0.65	0.60	1	3	4	-	Slightly Turbid
Potassium	0.001	0.92	0.86	0.80	0.72	0.70	0.66	1	1	2	1.14	Clear
Dihydrogen	0.002	0.94	0.88	0.84	0.78	0.74	0.74	"	"	"	1.20	"
Phosphate	0.005	0.94	0.86	0.82	0.74	0.70	0.68	"	"	"	1.17	"
	0.01	0.94	0.84	0.82	0.74	0.70	0.66	"	"	"	1.17	"
	0.2	0.84	0.80	0.76	0.72	0.64	0.62	"	"	"	1.06	"
	0.4	0.70	0.64	0.58	-	-	-	"	"	"	0.83	"
	0.6	0.66	0.60	0.56	-	-	-	"	"	"	0.80	"
	0.8	0.50	0.48	0.48	-	-	-	"	"	"	0.70	"
	1.0	0.46	0.44	0.44	-	-	-	"	"	"	0.63	"
	2.0	0.46	0.44	0.42	-	-	-	"	"	"	0.60	"
Sodium	0.001	0.92	0.88	0.84	0.76	0.72	0.58	1	1	2	1.2	Clear
Chloride	0.005	0.98	0.90	0.90	0.78	0.74	0.72	"	"	"	1.28	"
	0.01	0.96	0.86	0.82	0.78	0.74	0.72	"	"	"	1.17	"
	0.02	0.94	0.84	0.80	0.74	0.72	0.70	"	"	"	1.14	"
	0.20	0.80	0.76	0.70	0.64	0.64	0.64	"	"	"	1.00	"
	0.40	0.62	0.50	0.50	-	-	-	"	"	"	0.71	"
	0.60	0.56	0.46	0.40	-	-	-	"	"	"	0.57	"
	0.80	0.50	0.40	0.38	-	-	-	"	"	"	0.54	"
	1.0	0.40	0.40	0.38	-	-	-	"	"	"	0.54	"
	2.0	0.30	0.30	0.28	-	-	-	"	"	"	0.40	"

Table 6 : Effect of Aluminium Chloride and Calcium Chloride as Flocculating Agents on Benzoyl Metronidazole Suspension Stabilized with Sodium Carboxymethylcellulose.

Electrolyte	Concentration % w/v	Sedimentation Volume After Specified Time Intervals (days) 2	8	15	No. of inversion (days) 2	15	Degree of Flocculation after 15 days	Clarity of Supernatant
	0.000	0.86	0.74	0.70	1	3	-	Slightly Turbid
Aluminium Chloride	0.001	0.76	0.66	0.36	1	1	0.5	Turbid
	0.005	0.88	0.76	0.66	"	"	0.94	Turbid
	0.01	0.90	0.72	0.62	"	"	0.88	"
	0.05	0.88	0.74	0.66	"	"	0.94	"
	0.10	0.26	0.22	0.22	"	"	0.30	Very Turbid
	0.20	0.18	0.16	0.16	"	"	0.23	"
Calcium Chloride	0.001	0.88	0.74	0.60	1	1	0.86	Slightly Turbid
	0.005	0.86	0.70	0.60	"	"	0.86	"
	0.01	0.36	0.36	0.28	"	"	0.40	"
	0.05	0.22	0.20	0.18	"	"	0.25	"
	0.10	0.16	0.16	0.16	"	"	0.23	"
	0.20	0.12	0.11	0.10	"	"	0.14	Very turbid

Table 7 : The Sedimentation Volume of the Formulated Suspension.

Number of Batch	Mean Sedimentation Volume After Specified Time Intervals (days) 2	8	15	30	60	Number of inversion after(days): 2	15	60	Clarity of the Supernatant
Formula 1	0.96	0.86	0.85	0.78	0.73	1	1	2	Clear
Formula 2	0.96	0.89	0.88	0.76	0.71	1	1	2	Clear

Table 8 : Dissolution Rate Constant K (min^{-1}) of Formulated Benzoyl Metronidazole Suspension Freshly Prepared.

Formula No.	Bottle No.	Correlation Coefficient (r)	K X 10^2
1	1	0.9780	2.0469
	2	0.9829	2.0415
	3	0.9785	2.0879
	4	0.9860	2.0895
Mean	-	0.9838	2.0571
2	1	0.9898	1.8285
	2	0.9873	1.8253
	3	0.9813	1.7581
	4	0.9724	1.7844
Mean	-	0.9841	1.4807

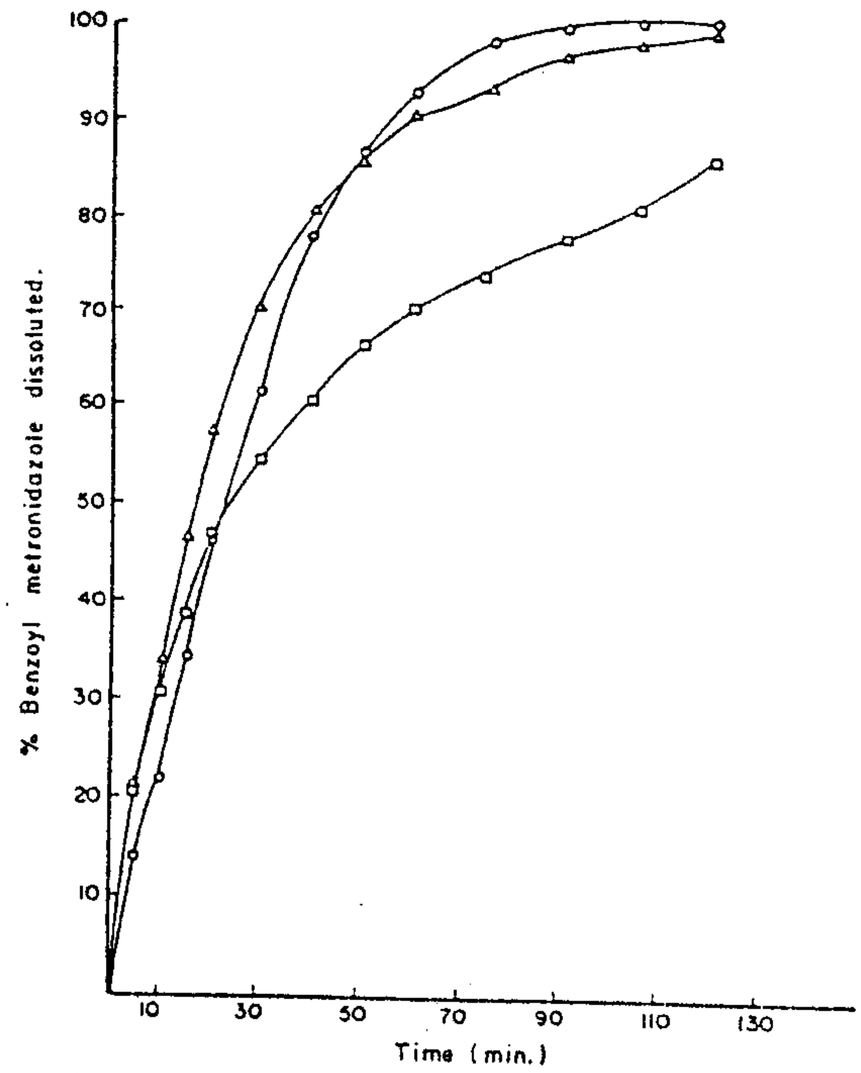

Fig.(1): Effect of particle size on the dissolution behaviour of benzoyl metronidazle powder.
o More than 90 um. ▲ 90 — 63 um.
o Less than 63 um.

Table 9 : Dissolution Rate Constant K (min^{-1}) of Formulated Benzoyl Metronidazole Suspension After Storage.

Formula No.	Bottle No.	Correlation Coefficient (r)	K X 10^2
1	1	0.9703	2.0559
	2	0.9880	1.9906
	3	0.9668	1.9832
	4	0.9727	2.0436
Mean	-	0.9972	1.9926
2	1	0.9703	1.8818
	2	0.9668	1.8081
	3	0.988	1.7826
	4	0.9727	1.7542
Mean	-	0.9656	1.7588

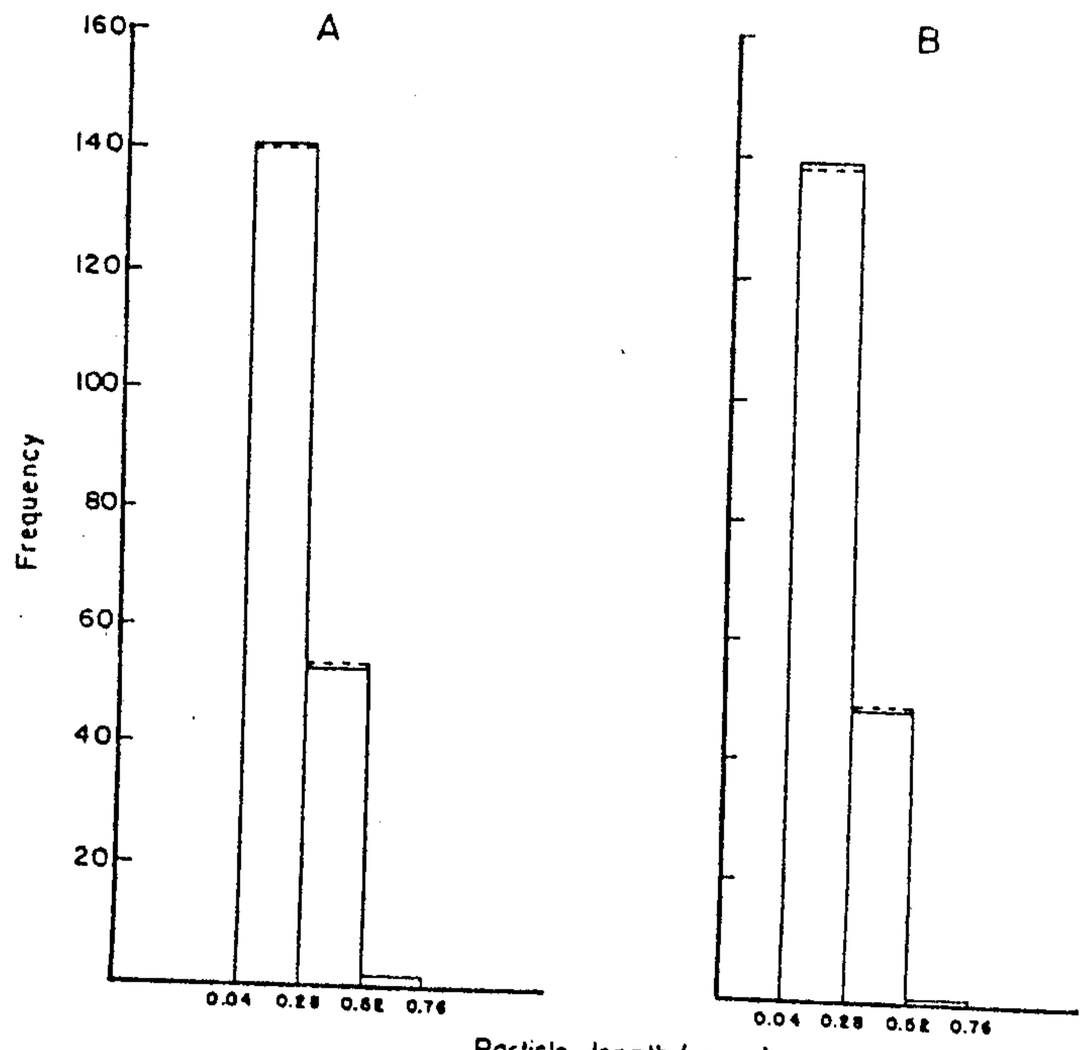

Fig.(2): Particle length distribution of formulated suspension before (——) and after (– – –) 12 monthes aging.
Benzoyl metronidazole suspension flocculated with
A Potassium dihydrogen phosphate.
B Sodium chloride.

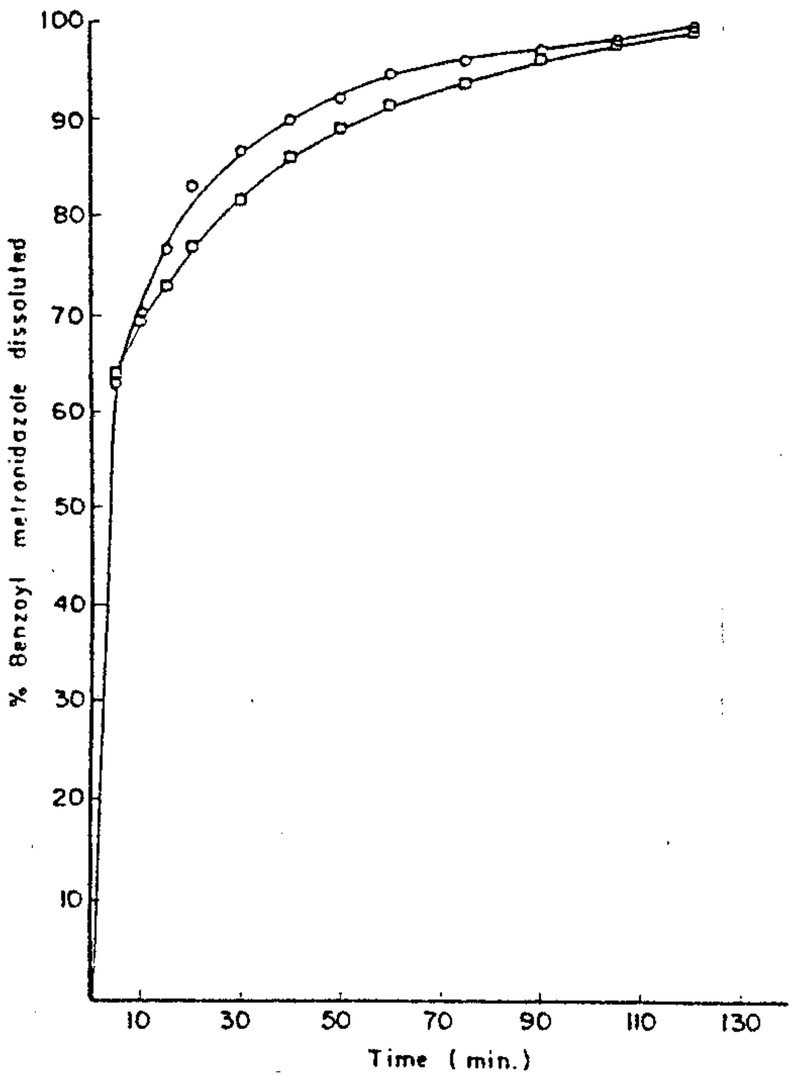

Fig. (3.): dissolution profile of benzoyl metroni_ dazole formulated suspension.
oFormula No.1 flocculated by potassium dihydrogen phosphate.
oformula No.2 flocculated by sodium chloride.

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صياغة وتقييم معلق بنزوات المترونيدازول

السيد على ابراهيم ـ سوزان شوقى طوس ـ تهانى حسن الفحام ـ مهاعبدالعظيم حسن

قسم الصيدلانيات ـ كلية الصيدلة ـ جامعة اسيوط ـ اسيوط

فى هذا البحث قد تم دراسة العوامل والمواد المختلفة التى تؤثر على صياغة معلق بنزوات المترونيدازول وقد اسفرت هذه الدراسة عن اختيارصيغتين وجد فيهما المعلق فى احسن صورة من الناحية الفيزيائية والكيميائية. وهاتين الصيغتين هما :

الاولى : تتكون من ٢ر / من التوين ٤٠ ، ١ / من كربوكس ميثيل سليلوز الصوديوم، ٠٠٢ر وفوسفات البوتاسيوم ثنائية الايدروجين .

والثانية : تحتوى على نفس المواد بالاضافة الى كلوريد الصوديوم (٠٠٥ر /) بدلا من فوسفات البوتاسيوم ثنائية الايدروجين بالاضافة الى المواد الحافظة للصيغتين .

وقد تم تقييم المعلق المحضر طبقا للمقاييس الاتية : حجم الراسب ـ سرعة الانتشار ـ كمية العقار الداخلة فى التركيب ـ معدل الذوبان ـ حجم الحسيمات .

وقد وجد ان المعلق المحضر يفوق فى صفاته ذلك المتوفر بالسوق والذى سبق دراسته فى بحث سابق حيث ان الطبقة المترسبة واحدة بعكس المعلق المتوفر بالسوق بأنه ينفصل الى طبقتين من الراسب احداهما تطفو الى اعلى بالاضافة الى ان المعلق المحضر اذا ترك يترك طبقة رائقة من السائل فوق طبقة الترسيب كذلك فان المعلق المحضر اظهر ثباتا فيزيائيا وكيميائيا . وقد استدل على الثبات الكيميائى باستعمال كروماتوجرافيا الطبقة الرقيقة وذلك عند تخزينه لفترة من الزمن قدرها اثنى عشرة شهرا .

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