Bull. Pharm. Sci., Assiut University,
Vol. 14, Parts 1&2, PP 61-73

DESIGN OF SUSTAINED RELEASE FORMULATIONS OF SALBUTAMOL II- CLAY SORBATE SYSTEMS

H. Abdel Monem Sayed, A.M. El-Sayed, A. Hamed Osman* and M. Fathy

Pharmaceutics Dept., Faculty of Pharmacy, Assiut University, Assiut, Egypt
** Chest. Dept., Faculty of Medicine, Assiut University, Assiut, Egypt*

ABSTRACT

Salbutamol is an effective drug in the treatment of bronchial asthma. The adsorption of salbutamol onto various clays viz., veegum HV, bentonite and magnesium trisilicate was investigated. The optimal conditions for loading the drug onto the clays were determined. The drug release from its sorbates indicates the need for a diffusion barrier to modify the drug release profile. Cellulose acetate butyrate at 1:1 core:coat ratio was used as a coating material. The coated drug sorbates offered an acceptable release profile of the drug. Coated sorbates prepared by using drug loaded onto veegum HV as the core were used to prepare a sustained release formulation of the drug. The formulation was tested in asthmatic patients and compared to the plain drug by measuring some pulmonary functions. The administration of the sustained release formulation twice daily gave the same or better improvement than that of the plain drug given three times a day.

INTRODUCTION

Laminar silicates belong to a group of clay minerals able to form sorbates with organic compounds by intercalation of the molecules into the interlayer space of the clay [1]. Owing to the structure and properties, montmorillonite clays show special feature in terms of interaction which permits its use as a support in sustained release formulations [1]. The utilization of the clays to achieve sustained release drug delivery systems have been reported [1-6].

Salbutamol as a beta-2 adrenoreceptor stimulant is usually used in the management of bronchial asthma. The plasma half life of salbutamol has estimated to range from about 2 to as much as 7 hours [7].

Bhalla and Sanzgiri [8] prepared two controlled release formulations of salbutamol based on hydroxypropyl methyl cellulose and its combination with guar gum. Shekhara and Gupta [9] prepared and evaluated prolonged release nylon microcapsules containing salbutamol. Babu and Khar [10] formulated peroral sustained release floating capsules containing salbutamol. Forni *et al* [11]. Prepared salbutamol microcapsules by a spray drying techinque.

In the present study, certain clays were utilized as sustained delivery carriers for salbutamol. A cellulose derivative was used to coat the drug sorbate in an attempt to modify the drug release profile. The final aim was to formulate sustained release products of the drug.

EXPERIMENTAL

Materials:

-Salbutamol sulphate (Sigma Co., St. Louis, U.S.A.).

-Veegum HV (Vanderbilt Chemical Co., Norwalk, Conn., U.S.A.)

-Bentonite (Sigma Co., St. Louis, U.S.A.).

-Magnesium trisilicate (E.Merck, Darmstadt, Germany)

-Cellulose acetate butyrate, CAB (Sci. Polymer Products Inc., Ontario, New York, U.S.A.).

-All other chemicals were analytical reagent grades and were used as received. Simulated gastric and intestinal fluids (U.S.P., XXI) without enzymes but containing 0.02% w/v Tween 80 were prepared.

Apparatus:

-Double beam Spectrophotometer UV-150-02 (Shimadzu, Japan).

-USP dissolution apparatus, model DT-06 (Erweka, Germany).

-Thermostatically controlled water bath fitted with horizontally moved mechanical shaker (Gfl, D.Burgwedel, Germany).

-Centrifuge, DT-51 (Germany).

-X-ray generator PW 1700/1710 diffractometer control, (Philips, Netherland).

-Vitalometer (Warren E.Collins. Inc., Braintree, Mass, U.S.A.).

-Wright peak flowmeter (Airmed Limited, Harlaw, England).

Procedure:

1-Adsorption Studies:

The study was carried out by treating the adsorbent (100 mg) with 50 ml of salbutamol solution in distilled water. After treatment the sample was centrifuged for 10 minutes at 3600 rpm. The concentration in the supernatant was measured spectrophotometrically at 296 nm after dilution with 0.1 N NaOH [8]. The amount of drug adsorbed onto the clay could be calculated. To determine the optimal conditions for loading the drug, the treatment was carried out under different processing variables:

(1)The time of contact was varied as follows: 5, 10, 15, 20, 30, 45 and 60 minutes.

(2)Temperature change at which the treatment occurs was 25, 30, 35, 40, 45 and 60°C.

(3)Shaking rate; 0, 10, 30, 50, 60 and 70 stroke/minute was tested.

(4)Different clays; veegum HV, bentonite and magnesium trisilicate, were used.

(5)The concentrations of the drug solution were; 5, 10, 20, 50, 125, 250, 500, 625, 750 and 875 mg/50 ml.

2-Preparation of drug sorbate

The amount of adsorbent (100 mg) was added to the drug solution (50 ml of 1% w/v) in a stoppered bottle. The preparations were shaken (30 storke/minute) at 25°C for 30 minutes. Each sample was centrifuged for 10 minutes at 3600 rpm. The residue was taken and dried at 50°C for 24 hours. The sample was ground and passed through sieve (63-um). Then, the sorbates were rotated end-over-end in a capped bottle for 10 minutes to ensure uniformity.

3- X-ray diffraction

The sorbate of both veegum HV and bentonite were tested. The samples (salbutamol sulphate, veegum HV, bentonite and drug sorbates) were dried completely to constant weight and finely pulverised before testing.

4-Coating of drug sorbates:

Sorbate samples loaded with drug, equivalent to 0.16, 0.15 and 0.13 g. of drug/g. of carrier in case of veegum HV, bentonite and magnesium trisilicate respectively were used. Cellulose acetate butyrate containing 10% w/w PEG 4000 was used as the coating material at core:coat ratio of 1:1. The adopted procedure was the emulsion-solvent evaporation process. The coating material was dissolved in acetone at 10% w/v concentration. The drug sorbate was dispersed in the coating solution. The dispersion was added while stirring to paraffin oil (1:3). Stirring was continued till complete evaporation of acetone. The formed microcapsules were separated by filtration using filter papers, washed with n-hexane and dried at room temperature. The dried microcapsules were fractionated into different sieve (five) fractions using a set of standard sieves.

5-Determination of micro-capsule drug content:

100 mg-samples representing the different sieve fractions were crushed in a mortar. Simulated gastric fluid was added to the mortar content. The content was quantitatively transferred to a volumetric flask. The flask was completed to volume by simulated gastric fluid. The drug concentration was determined spectrophotometrically at 276nm[8].

6-*In Vitro* release studies:

Release studies were carried out at 37°C in 200 ml of dissolution media. The USP standard apparatus, with teflon-coated paddles stirrers, at 50 rpm was used. Both of simulated gastric fluid and simulated intestinal fluid were used separately as the dissolution media. Each medium was used without enzymes but 0.02% w/v Tween 80 was added to overcome the poor wettability of the samples and make the solution more colsely resembling the surface tension of gastrointestinal fluid [12]. Accurately weighed samples (100 mg of microcapsules or 50 mg of drug sorbates) were added to the dissolution medium. Aliquots of 5 ml were withdrawn at intervals and replaced with similar volume of fresh medium. The amount of released drug was determined spectrophotometrically at 276 nm in case of simulated gastric fluid and at 296 nm in case of simulated intestinal fluid after dilution with 0.1 N NaOH [8].

7-Clinical Evaluation:

A sustained release formulation of salbutamol was prepared and filled into a hard gelatin capsule. The formulation was prepared so as to contain 2.26 mg of plain drug (initial dose) and an amount of microencapsulated sorbate equivalent to 4 mg of the drug (maintenance dose). The calculation was based on that the sustained release formulation contains 4 mg of each of initial dose and maintenance dose. The microcapsules prepared using CAB as the coating material and drug loaded onto veegum HV as the core at 1:1 core/coat ratio. Non-treated drug in 4 mg was also filled in hard gelatin capsules and used as control. The preparations were tested in six hospitalized patients suffering from reversible chronic airflow obstruction. No other medications were taken during the study. Each subject received one capsule of plain drug three times daily for one week and one capsule of the sustained release formulation twice daily for another week. The forced expiratory volume in one second (FEV_1) and the peak

expiratory flow rate (PEFR) were measured using Collins vitalometer and wright peak flowmeter respectively. The measurements were determined before drug administration and then through three readings taken at 8 A.M., 2 P.M. and 8 P.M. during medication. Any signs of improvement or side effects were observed in patients during the period of treatment.

RESULTS AND DISCUSSION

In an attempt to design sustained release formulations of salbutamol, the drug was loaded onto three selected clays namely, veegum HV, bentonite and magnesium trisilicate, characterized with their adsorptive properties. Several variables were tested to determine the optimum conditions for drug loading.

The adsorption of the drug was rapid with the three tested clays. An equilibrium was attained after 20 minutes, therefore, a time of contact of 30 minutes was regarded to be adequate period.

The increase in the temperature of interacting medium was found to increase the amount of drug adsorbed in case of bentonite while, the increase in temperature decreased the amount adsorbed in case of veegum HV and magnesium trisilicate (Table 1). The increase in the amount adsorbed can be attributed to the activation of the exchange process. The behaviour exhibited by veegum can be attributed to the acceleration in its hydration with the formation of high viscous dispersion upon increasing temperature [13]. An effect which retards the exchange process. The decreasing effect in case of magnesium trisilicate can be explained by the increase in the extent of hydration of magnesium trisilicate by heat. As a result a temperature of 25°C was regarded as an ideal condition for drug loading.

The shaking rate was found to have insignificant effect on the amount of drug adsorbed. A rate of 30 stroke/minute was used for the preparation of drug sorbate.

The effect of loading solution concentration was studied. The adsorption data were plotted according to Langmuir equation [14] (Figure 1).

$$Ce/Y = 1/ab + Ce/b$$

where Ce is the equilibrium concentration of solute, Y is mg of solute adsorbed per g. of adsorbent, b is a constant called the adsorptive capacity and a is another constant.

Linear adsorption isotherms with a slope of 1/b and an intercept of 1/ab were obtained (Figure 1). The (b) values were calculated as the reciprocal of the slope of the linear plots. The calculated values were found to be 192.11, 159.52 and 156.43 in cases of veegum HV, bentonite and magnesium trisilicate reapectively. The (b) value is a good measure of adsorptive capacity. it is worthy to note that the amount of drug adsorbed was found to be constant upon increasing the initial drug concentration beyond certain values. The maximum loaded amount obtained was 185, 150 and 140 mg/g. in cases of veegum HV, bentonite and magnesium trisilicate respectively. These values correspond to initial drug concentrations of 750. 500 and 625 mg/50 ml respectively.

Drug sorbates were prepared under the determined optimal specified conditions and 1% w/v drug concentration. The weight ratios of the prepared sorbates (g. of drug/g. of adsorbent) were found to be 0.16/1, 0.15/1 and 0.13/1 in cases of veegum HV, bentonite and magnesium trisilicate.

To confirm the adsorption of salbutamol into the interlayer space of montmorillonite, X-ray diffractograms of each of salbutamol sulphate, veegum HV and bentonite, as well as, their drug sorbates were studied. In this study, magnesium trisilicate was not included as it is not considered as a laminated clay, in addition that its adsorption is mainly physical. Figure 2 shows that there is a significant decrease in the intensity of drug peaks after its interaction with clays. This indicates the entrance of the drug molecules into the interlayer space of the clay.

The *in vitro* dissolution studies of the prepared sorbates (Table 2) show that, the extent of drug release from its sorbates was in the order magnesium trisilicate > veegum HV > bentonite. The high extent in case of magnesium trisilicate confirms the physical adsorption nature of its sorbate. In spite that the release from the veegum HV or bentonite sorbates is being relatively slow, it is still at rate not suitable for sustained release products. This explains the entrance of drug molecules into the interlayer space of these clays in a manner that allows the drug molecules to enter in and leave out without difficulty. The release patterns of the drug from its sorbates necessitate the need for a diffusion barrier to modify these patterns.

Cellulose acetate butyrate was used to coat the drug sorbates at 1:1 core:coat ratio applying the microencapsulation techinque. The determined drug content (Table 3) as well as the electron micrographs of the prepared microcapsules (Figure 3) indicate the effeciency of the adopted procedure. The yield was found to be not less than 93% at any of the tested clays.

Table 4 shows that the microcapsule size and size distribution were not significantly changed by the use of different clay sorbates as the core.

The results of drug release from the microencapsulated sorbates (Figures 4-6) show that, the larger the microcapsule size, the faster is the release rate of the drug thereof. A result which may be attributed to a larger cores and subsequently thinner coat in case of large microcapsules.

Generally, the release rates from the uncoated or coated sorbates were faster in simulated gastric fluid than those in simulated intestinal one. The results can be attributed to the enhanced solubility of the basic drug in the acidic medium.

Drug sorbates prepared by loading the drug onto veegum UV exhibited the most acceptable release pattern of the drug when used as core materials. The microcapsules prepared by using any of the other two clays showed undesirable release profiles. In this respect, in case of bentonite, a very slow release rate where less than 50% of the drug was released after 8 hours. At the same time, with magnesium trisilicate although the amount released after 8 hours was in the range of 60-69%, a biphasic release pattern with a non predictable rate was exhibited.

A sustained release product of salbutamol was formulated using the microcapsules prepared by drug loaded onto veegum HV as the core. The formulation was clinically evaluated in asthmatic patients. Two parameters related to the lung function, namely, the forced expiratory volume in one second (FEV_1) and the peak expiratory flow rate (PEFR) were measured. The FEV_1 was re-

ported as the best single test for assessing bronchodilator response[15,16].

From the data presented in Table 5 and 6, it can be seen that, there was a gradual improvement in the pulmonary functions. The improvement reaches its maximum values after the fourth day for both plain and sustained release formulation. The sustained release formulation started with higher values than the plain drug. A result which can be attributed to a constant level of the drug produced by the sustained release formulation compared to a fluctuated one due to plain drug. Lower pulmonary function values were recorded in the morning. A result which can be explained on the base of circadian rythm of the bronchial asthma [17]. The effect was minimized upon treatment with the sustained release formulation.

Clinically, it was observed that there are subjective improvement of dyspnea and wheezes. Also, neither asthmatic attacks nor side effects were observed during the treatment period.

Table 1: Amount of Salbutamol Sulphate Adsorbed, (mg/g.) of Adsorbents, As a Function of Temperature.

Temperature °C	Salbutamol Adsorbed on the Following Clays		
	Veegum Hv	Bentonite	Magnesium Trisilicate
25	64.45	71.11	25.21
30	62.80	72.80	24.30
35	60.18	74.45	22.60
40	57.09	74.30	22.60
45	55.42	76.35	20.22
60	54.23	76.83	16.51

Initial drug concentration 1:25 mg/50 ml.

Table 2: *In Vitro* Release of Salbutamol from its Sorbates Prepared by the Use of Various Clays.

Clay used		Drug Released (% w/w) after the Following Specified Time Intervals (Hours)							
		0.5	1	1.5	2	3	4	6	8
Veegum HV	A	83.18	84.85	90.46	92.44	95.91	100		
	B	61.56	67.61	74.70	75.05	76.86	80.40	90.10	100
Bentonite	A	58.40	69.78	75.85	87.50	98.70	99.87		
	B	51.64	56.29	65.80	72.64	90.80	93.00	93.18	100
Magnesium Trisilicate	A	69.00	82.69	94.99	98.42	100	100		
	B	61.01	66.70	82.40	31.70	91.99	94.33	97.25	100

A = In simulated gastric fluid.
B = In simulated intestinal fluid.

Table 3: Drug Content of Salbutamol Microcapsules Prepared by the Use of PEG-Treated Cellulose Acetate Buytyrate as the Coating Material and the Drug Loaded onto the Clay as the Core.

Microcapsule Fraction Size um	Drug Content (% w/w) on Using The Following Clays		
	Veegum HV	Bentonite	Magnesium Trisilicate
90-200	6.85	6.43	5.81
200-315	6.92	6.50	5.93
400-630	6.99	6.52	6.06

Table 4: Frequency Distribution of Salbutamol Microcapsules Prepared by the Use of PEG-Treated Cellulose Acetate Buytyrate as the Coating Material and the Drug Loaded onto the Clay as the Core..

Microcapsule Fraction Size um	Drug Content (% w/w) on Using The Following Clays		
	Veegum HV	Bentonite	Magnesium Trisilicate
90-200	20.85	25.58	27.64
200-315	27.92	26.84	33.34
315-400	11.51	11.42	9.38
400-630	22.66	23.75	15.39
630-710	17.06	12.41	14.25

Table 5: Absolute and Percent Predicted Forced Expiratory Volume in One Second (FEV_1) after Oral Administration of Salbutamol.

Day	Formulation	8 A.M.		2 P.M.		8 P.M.	
		Absolute	% Predicted	Absolute	% Predicted	Absolute	% Predicted
1st	P	1.47 ± 0.06	46.79 ± 3.26	1.51 ± 0.09	48.25 ± 3.62	1.58 ± 0.20	50.34 ± 6.08
	S	2.15 ± 0.08	67.19 ± 2.21	2.25 ± 0.07	70.32 ± 2.21	2.25 ± 0.07	70.28 ± 2.16
2nd	P	1.70 ± 0.10	54.27 ± 5.25	1.79 ± 0.13	57.10 ± 5.12	1.84 ± 0.15	58.68 ± 5.13
	S	2.25 ± 0.07	70.32 ± 2.21	2.35 ± 0.07	73.44 ± 2.21	2.45 ± 0.07	76.57 ± 2.21
3rd	P	2.00 ± 0.10	63.77 ± 4.15	2.04 ± 0.14	65.02 ± 4.78	2.19 ± 0.27	69.87 ± 8.32
	S	2.25 ± 0.21	70.32 ± 6.63	2.35 ± 0.07	75.01 ± 4.42	2.45 ± 0.07	76.57 ± 2.21
4th	P	2.13 ± 0.15	68.00 ± 5.18	2.23 ± 0.23	71.12 ± 6.52	2.30 ± 0.20	73.22 ± 4.32
	S	2.25 ± 0.21	70.32 ± 6.63	2.45 ± 0.07	76.57 ± 2.21	2.45 ± 0.07	76,57 ± 2.21
5th	P	2.27 ±0.06	72.20 ± 0.98	2.40 ± 0.10	76.44 ± 1.81	2.40 ± 0.10	76.44 ± 1.81
	S	2.35 ± 0.07	74.17 ± 1.18	2.45 ± 0.07	76.57 ± 2.21	2.45 ± 0.07	76.57 ± 2.21
6th	P	2.27 ± 0.06	72.20 ± 0.78	2.40 ± 0.10	76.55 ± 1.81	2.40 ± 0.10	76.44 ± 1.81
	S	2.30 ± 0.14	73.44 ± 6.63	2.45 ± 0.07	76.57 ± 2.21	2.45 ± 0.07	76.57 ± 2.21
7th	P	2.27 ± 0.06	72.20 ± 0.98	2.40 ± 0.10	76.44 ± 1.81	2.40 ± 0.10	76.44 ± 1.81
	S	2.30 ± 0.14	73.44 ± 6.63	2.45 ± 0.07	76.57 ± 2.21	2.45 ± 0.07	76.57 ± 2.21

EFV_1 pre-drug = 1.47 ± 0.06 litre
P : Plain drug

FEV_1 Predicted = 3.14 ± 0.12 litre
S : Sustained release formulation

Table 6: Absolute and Percent Predicted Peak Expiratory Flow Rate (PEFR) after Oral Administration of Salbutamol

Day	Formulation	8 A.M.		2 P.M.		8 P.M.	
		Absolute	% Predicted	Absolute	% Predicted	Absolute	% Predicted
1st	P	310 ± 30	56.43 ± 8.03	360 ± 40	58.60 ± 7.27	370 ± 40	59.67 ± 7.39
	S	410 ± 40	59.68 ± 13.68	440 ± 40	70.97 ± 6.84	460 ± 30	74.20 ± 4.56
2nd	P	370 ± 50	60.78 ± 8.15	380 ± 50	62.40 ± 8.93	400 ± 50	65.12 ± 8.98
	S	470 ± 50	75.00 ± 5.70	480 ± 20	76.61 ± 3.42	490 ± 15	79.04 ± 2.28
3rd	P	410 ± 40	66.74 ± 8.09	430 ± 50	69.46 ± 8.71	440 ± 40	72.15 ± 6.68
	S	480 ± 40	76.62 ± 5.71	480 ± 30	72.42 ± 4.57	500 ± 20	79.84 ± 3.42
4th	P	450 ± 50	73.25 ± 9.08	470 ± 40	75.95 ± 7.63	490 ± 20	80.26 ± 4.92
	S	480 ± 30	77.42 ± 4.57	480 ± 30	72.42 ± 4.57	500 ± 20	79.84 ± 3.42
5th	P	470 ± 60	75.93 ± 10.84	480 ± 50	78.66 ± 9.13	500 ± 30	81.08 ± 4.42
	S	480 ± 30	77.42 ± 4.57	480 ± 30	77.42 ± 4.57	500 ± 20	79.84 ± 3.42
6th	P	470 ± 60	75.93 ± 10.84	480 ± 50	78.66 ± 9.13	500 ± 30	81.08 ± 4.42
	S	480 ± 20	77.42 ± 4.72	480 ± 30	77.42 ± 4.57	500 ± 20	79.84 ± 3.42
7th	P	470 ± 60	75.93 ± 10.84	480 ± 50	78.66 ± 9.13	500 ± 30	81.98 ± 4.42
	S	480 ± 20	77.42 ± 4.72	480 ± 30	77.42 ± 4.57	500 ± 20	79.84 ± 3.42

PEFR Pre-drug = 350 ± 50 Litre/Minute
PEFR Predicted = 620 ± 10 Litre/Minute
P : Plain drug
S : Sustained release formulation

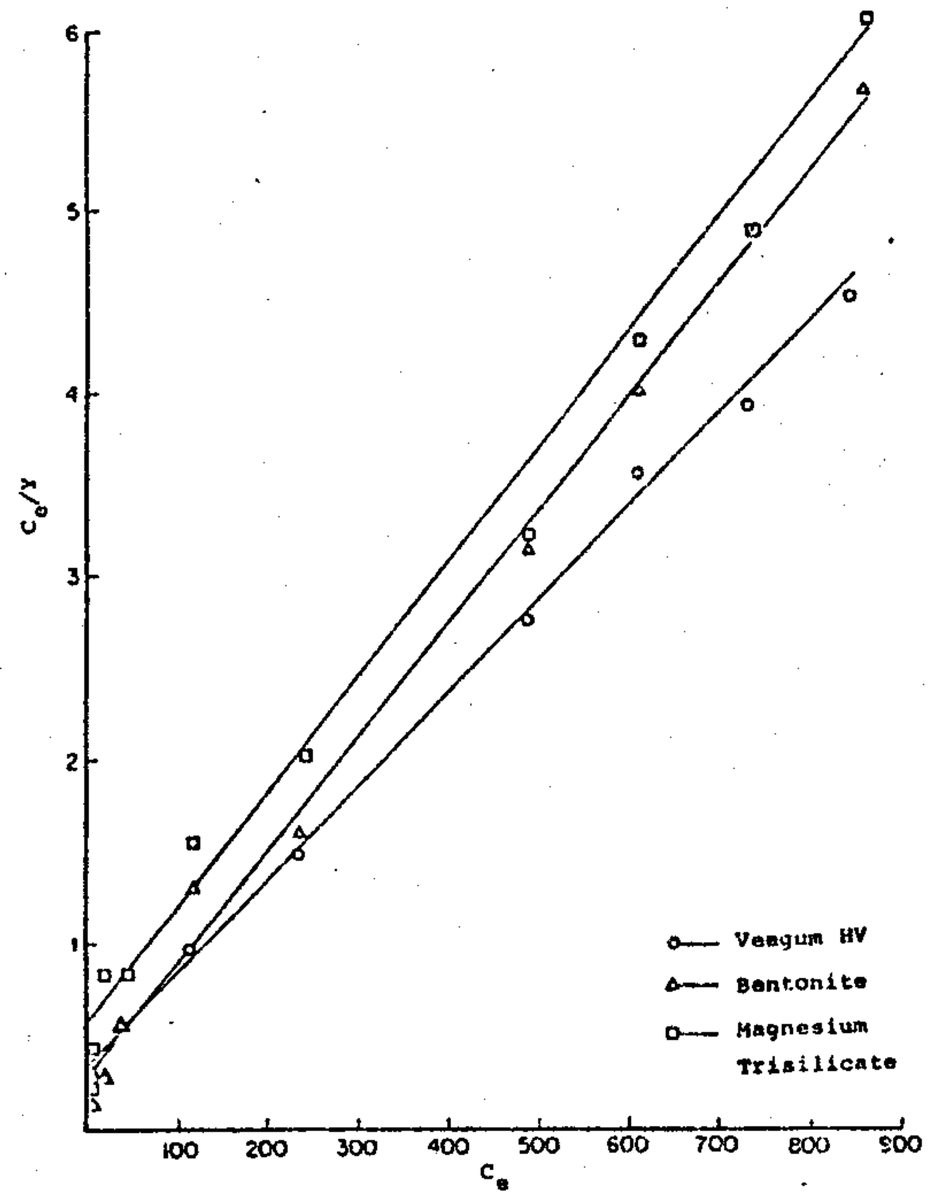

Figure 1: Langmuir Isotherm for Adsorption of Salbutamol Sulphate by Different Adsorbents.

C_e : Concentration of Salbutamol Sulphate at Equilibrium mg/50 ml.

Y : Milligrames of Salbutamol per gram of adsorbent.

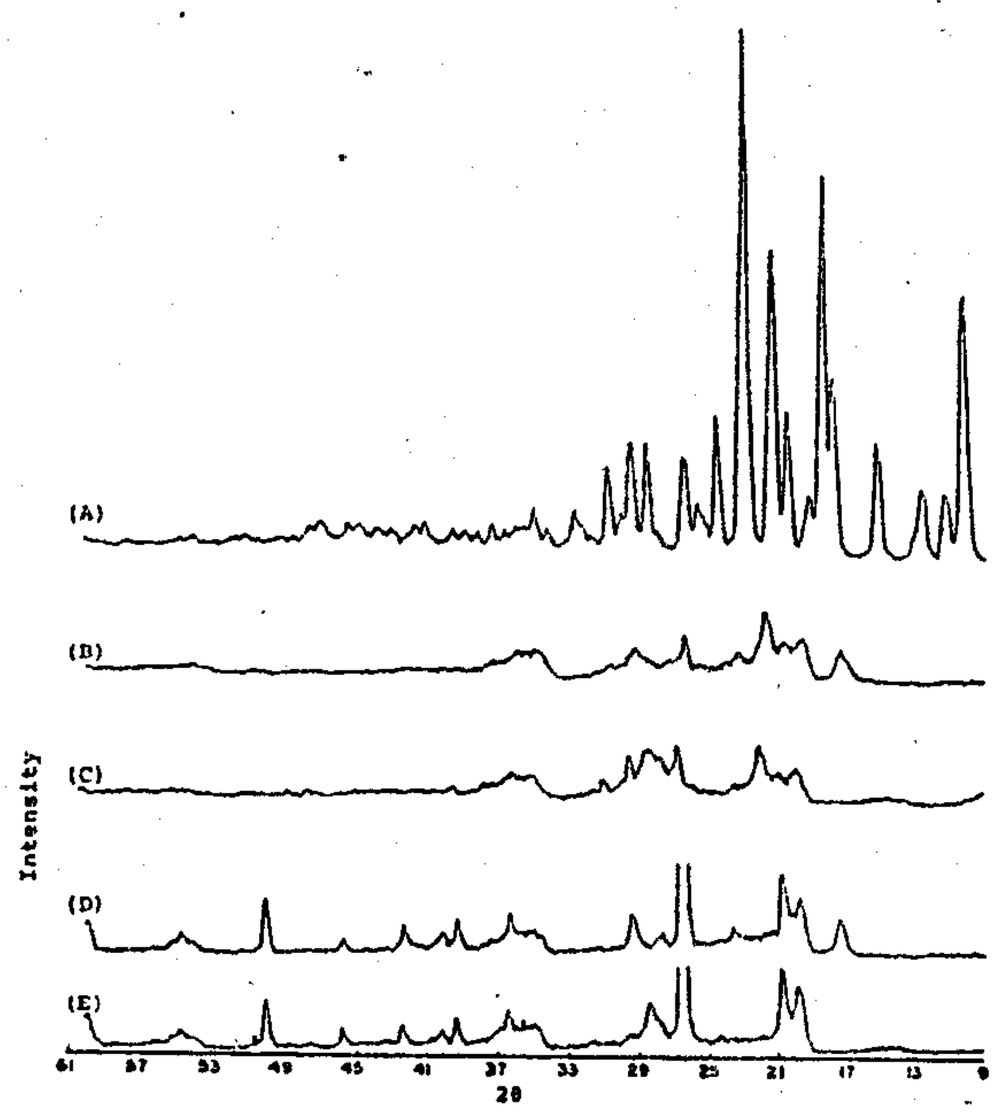

Figure 2: X-Ray Diffraction Analysis :

(A) Salbutamol Sulphate, (B) Salbutamol-Veegum HV Sorbate, (C) Veegum HV (D) Salbutamol Bentonite Sorbate and (E) Bentoinite.

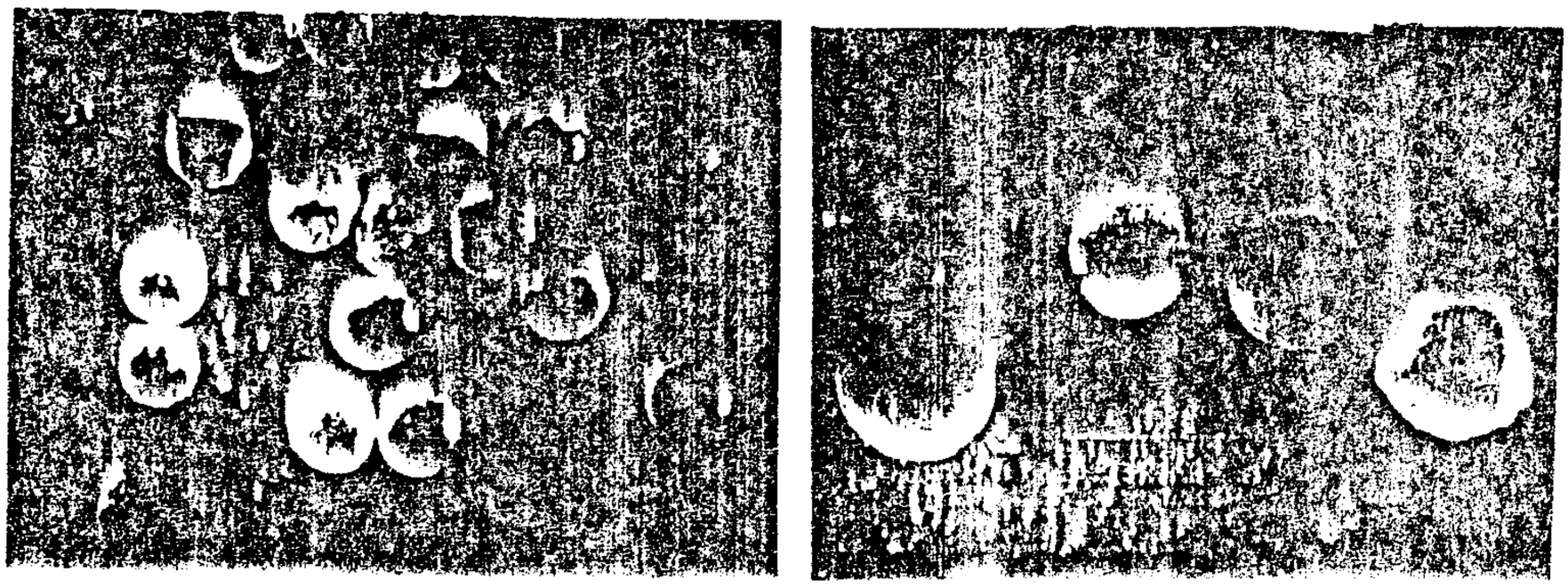

Figure 3 : Electron Scanning Micrographs of Salbutamol Microcapsules Prepared by the Use of Cellulose Acetate Butyrate as the Coating Material and Drug Loaded onto Clay as the Core.

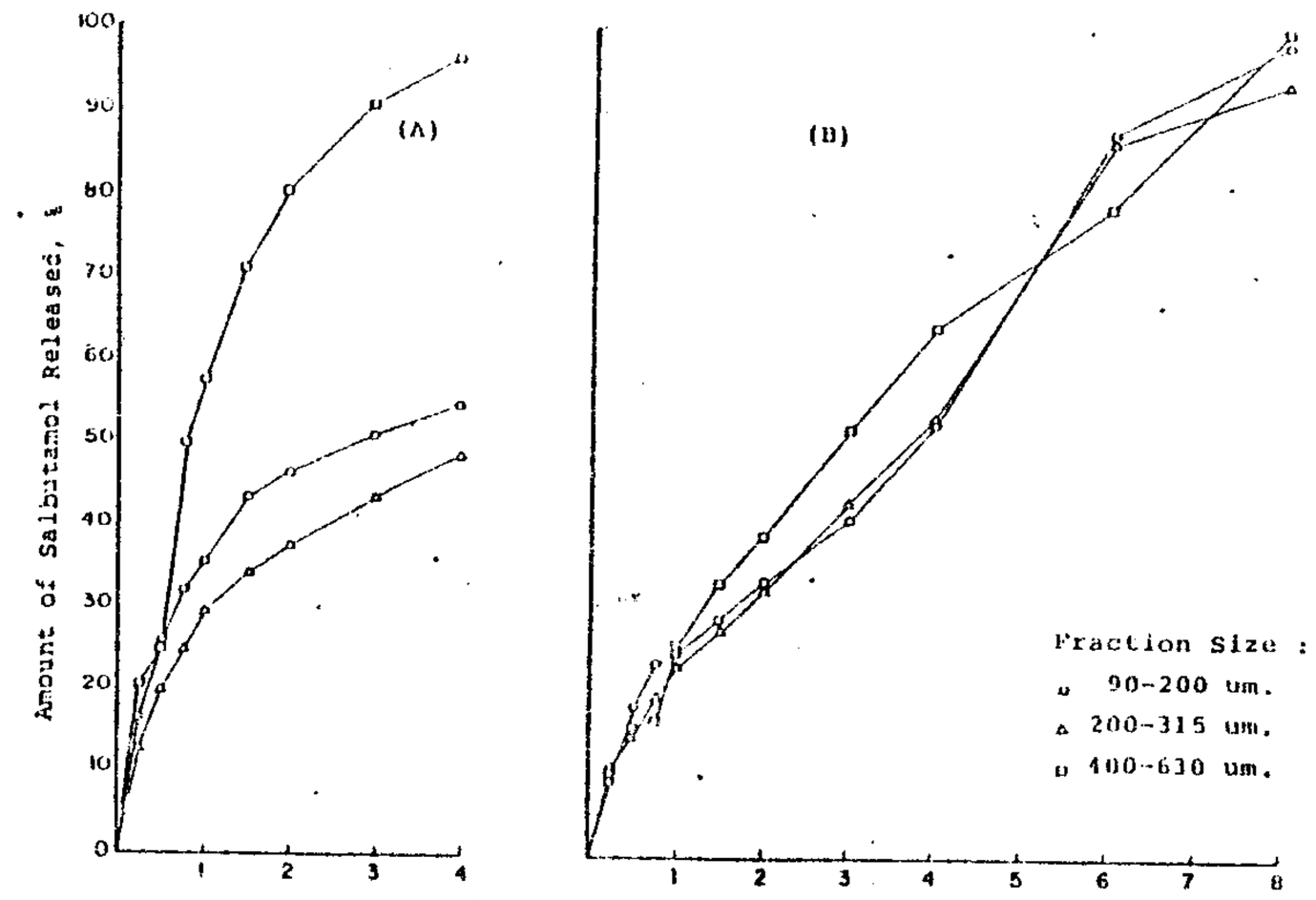

Figure 4 : In-Vitro Release of Salbutamol from its Microcapsules Prepared Using PEG-Treated Cellulose Acetate Butyrate as the Coating Material and Drug Loaded onto Veegum HV as the Core.

Key :
(A) in Simulated Gastric Fluid.
(B) in Simulated Intestinal Fluid.

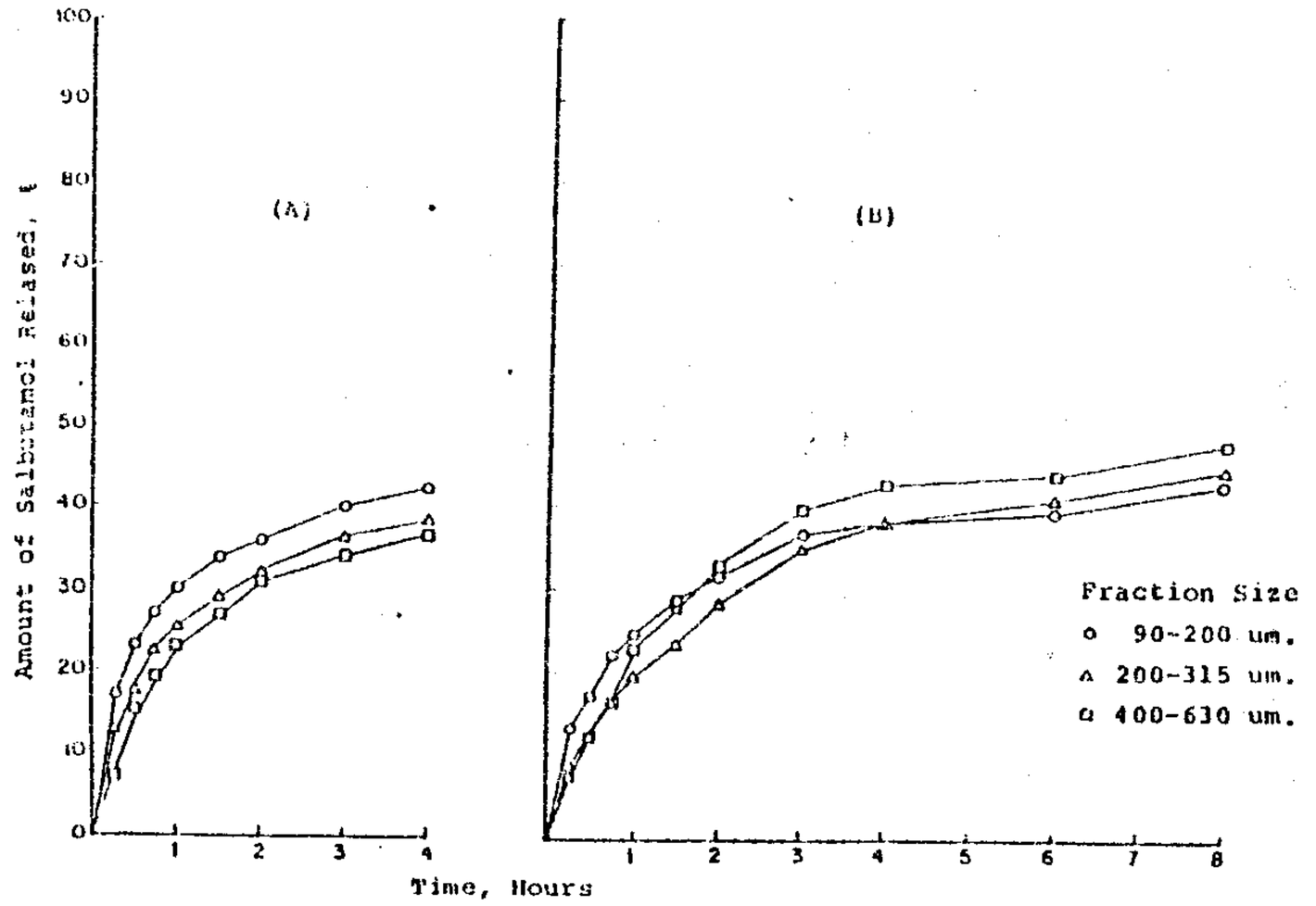

Figure 5 : In-Vitro Release of Salbutamol from its Microcapsules Prepared using PEG-Treated Cellulose Acetate Butyrate as the Coating Material and Drug Loaded onto Bentonite as the Core .

Key : (A) in Simulated Gastric Fluid.
(B) in Simulated Intestinal Fluid.

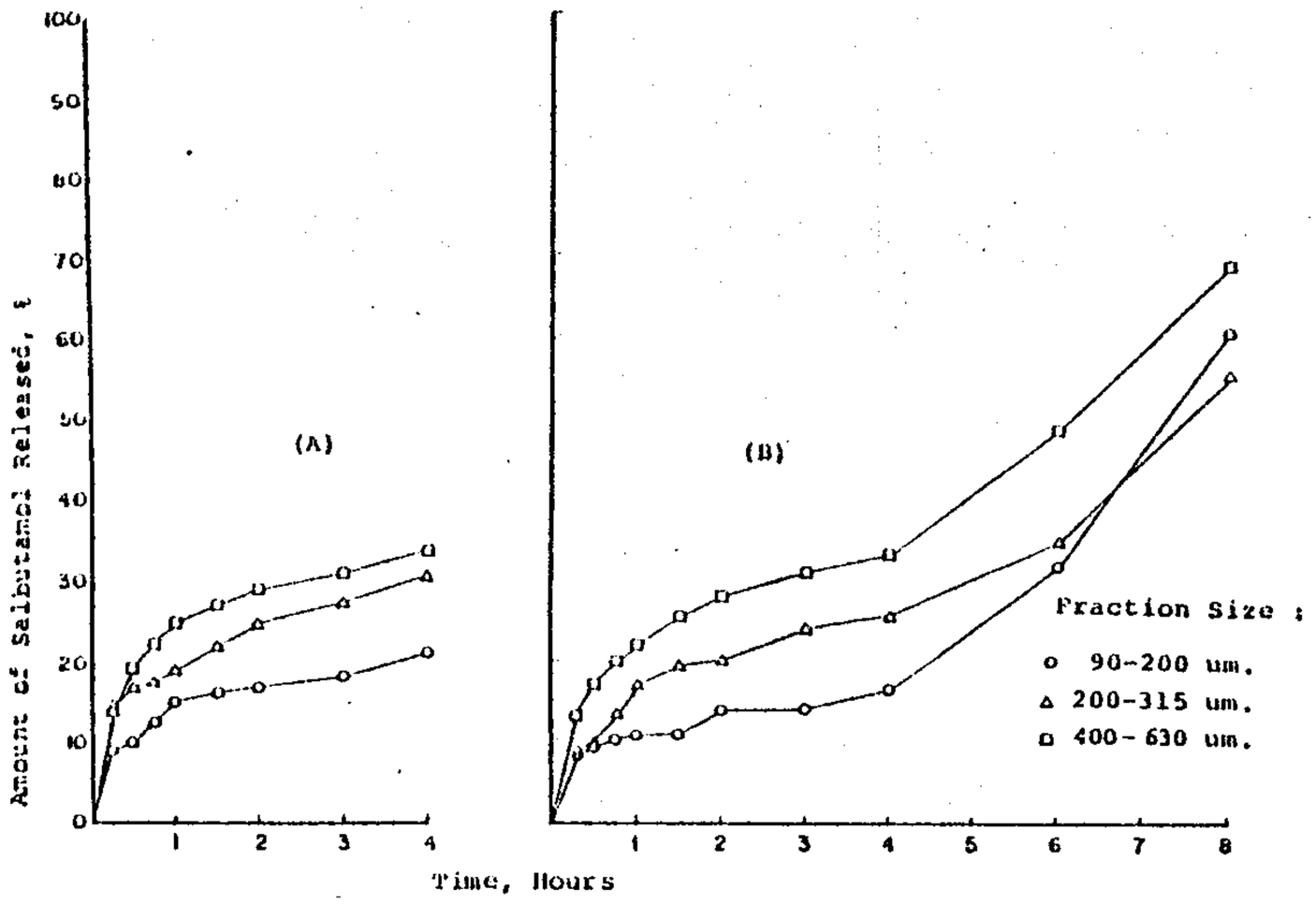

Figure 6 : In-Vitro Release of Salbutamol from its Microcapsules Prepared Using PEG-Treated Cellulose Acetate Butyrate as the Coating Material and Drug Loaded onto Magnesium Trisilicate as the Core.

Key:

(A) in Simulated Gastric Fluid.

(B) in Simulated Intestinal Fluid.

REFERENCES

1-M.L.Salayero, M.J.Sanchez, C.M.Sanchez and A.Dominguez-Gil;, Drug Dev. Ind. Pharm., 11, 1909 (1985).

2-J.W.McGinity and J.L.Lach, J.Pharm. Sci., 66, 63 (1977).

3-M.T.Vicente Hernandez, Thesis Doctoria., Facultad de Farmacia, Universidad de Salamanca (1981). Theough Drug Dev. Ind. Pharm., 11, 1909 (1985).

4-M.S.Stul, D.P.Vliers and J.B.Uytterhoven, J. Pharm. Sci., 73, 1372 (1984).

5-C.Echert-Lill, N.A.Lill, W.Endress and H.Rupprecht, Drug Dev. Ind. Pharm., 13, 1511 (1987).

6-F.Forni, V.Iannuccelli, G.Coppi and M.T.Bennabei, Arch. Pharm., 322,789 (1989).

7-W.Martindale, Ed., "The Extrapharmacopoeia", 29 th Ed., The Pharmaceutical Press, London (1980) P. 1480.

8-H.L.Bhalla and Y.D.Sanzgiri, Indian J. Pharm., 49, 22 (1987).

9-C.Shekkara and B.K.Gupta, East. Pharm., 31, 129 (1988).

10-V.B.M.Babu and R.K.Khar, Pharmazie, 45, 268 (1990).

11-F.Forni, G.Coppi, M.A.Vandelli and M.T.Bernabei, Inter. J. Pharm., 60, 83 (1990).

12-Y.Pongpaibul, K.Marruyama and M.Iwatsuru, J. Pharm. Pharmacol., 40, 530 (1988).

13-W.Martindal, Ed., "The Extrapharmacopoeia", 29 th Ed., The Pharmaceutical Press, London (1989) P. 1433.

14-I.Langmuir, J. Amer. Chem. Soc., 39, 1484 (1917).

15-R.W.Light, S.A.Conaed and R.B.George, Chest 72, 512 (1977).

16-R.Berger and D.Smith, Chest 93, 541 (1988).

تصميم صياغات ممتدة المفعول لصياغات السلبيوتامول

٢ - استخدام الطفليات

حسين عبدالمنعم سيد - احمدمصطفى السيد - احمدحامد عثمان*- محمدفتحى محمد

قسم الصيدلانيات - كلية الصيدلة - جامعة اسيوط

*قسم الامراض الصدرية - كلية الطب - جامعة اسيوط

فى محاولة لتصميم صياغات ممتدة المفعول لعقار السلبيوتامول المستخدم كموسع للشعب الهوائية تم تحميل العقار على بعض الطفليات المعروفة بخصائصها الامتزازية متمثلة فى كل من الفيجم والبنتونيت وثلاثى سيليكات الماغنيسيوم حيث تم دراسة العديد من المتغيرات للوصول الى انسب ظروف للتحميل .وبدراسة معدلات انطلاق العقار من هذه المحملات وجد انها لاتفى بعمل صياغات ممتدة المفعول . لذا تم حوصلة هذه المحملات لتعطى معدلات انطلاق مناسبة تماما . وتم صياغة محملات الفيجم المحوصلة فى اشكال ممتدة المفعول وتقييمها علاجيا فى عديد من مرضى الربو الشعبى حيث اظهرت نتائج مرضية .

received in 10/4/1991 - accepted in 17/6/1991