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INFLUENCE OF AGING ON THE PHYSICAL CHARACTERISTICS OF AMPICILLIN SUPPOSITORIES

E.A.Hosny, A.A.Kassem and H.H.El-Shattawy
Faculty of Pharmacy , Al-Azhar University , Cairo , Egypt.

ABSTRACT

This part of study of in-vitro and in-vivo release of ampicillin suppositories details the effect of aging on release of both anhydrous ampicillin and ampicillin sodium from suppositories of different formulations. It also details the effect of aging on some of the physical characteristics of these suppositories. The prepared suppositories were stored in a refregirato at 4^0c and tested fresh and at 80, 145 and 240 days old. All the tested suppositories disintegrate within a resonable time (6 -9 min.) and showed nearly no change in the disintegration time after storage for 240 days. Also, aging had no effect on the dissolution time of polyethylene glycol. Aging caused no discoloration or crystal growth of the medicament on the surface of suppositories. Aging had an obvious effect on hardness and decreased the release rate of both anhydrous ampicillin and ampicillin sodium from all the tested suppositories.

INTRODUCTION

A prediction of the life of the product may be made by accelerating the decomposition process and extrapolating the results to normal storage conditions. Nevertheless, accelerated storage tests cannot be expected to

replace the conventional stability testing for the product finally marketed, althought they do minimize the effort of testing new formulations.

Ampicillin degrades to different products in aqueous solution. Concentrated solutions of ampicillin form polymers [1] which were seperated according to molecular size by gel filtration on acrylamide gel column[2]. Monomeric ampicillin retained full activity after having been passed through an acrylamide gel column. Polymers separated from aged ampicillin solution by gel filtration were found to be devoid of antibacterial activity.

In a study of the kinetics of degradation of ampicillin in solution , minimum hydrolysis occurred at pH 5.85 and maximum stability at pH 4.85 [3].

Sodium ampicillin was most stable at pH 7.5. The rate of degradation increases as pH varies above or below that value [4]. Freezing at -20^{0}c to -78^{0}c, generally increased the degradation of 1 % sodium ampicillin solution and decreased the degradation in 25 % solution[5].

This study discusses how aging affect the physical parameters of ampicillin suppositories and stability of ampicillin in the selected bases.

METHODS

Preparation of Suppositories

The suppositories were prepared adopting the fusion method.

Dissolution Time

The time for a water soluble suppository to dissolve completely in 10 ml of water was determined at 37^{0}c with agitation every 2 minutes.

Disintegration Time

This was carried out using Erweka melting time tester [6], the time required for complete liquifaction of suppositories at 37^{0}c was recorded.

Mechanical Strength

The test was carried out at 25^{0}c using Erweka breaking strength tester measuring the weight under which the suppository collapse.

In-Vitro Release

The in -vitro release study of ampicillin was done using a modification of the United States Pharmacopeia rotating basket method [7] using 200 ml

TABLE 1

Physical Characteristics Of Fresh and Stored Ampicillin Suppositories.

Base	Medicament	Disintegration time(min.)		Dissolution time(min.)		Hardness (kg.)	
		F.	S.	F.	S.	F.	S.
Novata BD	--	6.0	7.0	--	--	4.2	4.8
Novata BD	anh.amp.	6.0	7.0	--	--	4.2	>5.6
Novata BD	amp.sod.	6.0	6.5	--	--	4.8	>5.6
Witepsol H_{15}	--	10.0	11.0	--	--	4.2	4.8
Witepsol H_{15}+0.1% polysorbate 80	--	7.0	8.0	--	--	4.3	4.5
Witepsol H_{15}	anh.amp.	7.0	8.0	--	--	4.0	4.4
Witepsol H_{15}	amp.sod.	9.0	10.0	--	--	5.3	>5.6
Witepsol H_{15}+0.1 polysorbate 80	amp.sod.	9.0	10.0	--	--	4.4	4.6
PEG	amp.sod.	--	--	32.0	32.0	5.6	>5.6

F. = Fresh
S. = Stored for 240 days.

distilled water maintained at 37 + 0.5 ^{0}c as the dissolution medium. Samples were withdrawn after 2 hours using 1.0 ml volumetric pipette . Ampicillin was assayed by a modification of Smith et al [8] assay method.

RESULTS AND DISSCUSION

Table 1, report the disintegration time, dissolution time and hardness of all the tested suppositories when prepared fresh and after storage for 8 month. All the tried suppositories formulated with Witepsol H_{15}, Witepsol H_{15} + 0.1% polysorbate 80, and Novata BD, disintegrated within 6-9 min. and showed nearly no change in the disintegration time after storage.

TABLE 2

Stability of Ampicillin in Different Suppository Bases

Base	Medicament	Ampicillin Retained (%)			K	$t_{1/2}$	t_{90}
		80	145	240	$(days)^{-1}$	(days)	(days)
Witepsol H_{15}	anh.amp.	16.82	67.77	85.47	0.008	86.56	13.16
Novata BD	anh.amp.	60.00	77.90	92.20	0.011	65.79	10.00
Witepsol H_{15}	amp.sod.	24.03	34.30	46.29	0.003	253.50	38.55
Witepsol H_{15}+0.1% polysorbate 80	amp.sod.	17.70	27.74	36.70	0.001	328.30	49.92
Novata BD	amp.sod.	21.38	31.59	34.70	0.003	270.63	41.15
PEG	amp.sod.	43.87	63.47	77.06	0.006	112.41	17.10

The dissolution time of ampicillin sodium / polyethylene glycol was 32 min. and aging had no efffect on this parameter.

Aging had obvious effect on hardness. The hardness of plain Novata BD was 4.2 kg and when formulated with anhydrous ampicillin and ampicillin sodium was 4.2 and 4.8 kg respectively which on storage became harder (> 5.6 kg).

The hardness of Witepsol H_{15} was 4.2 kg and when formulated with anhydrous ampicillin was 4.0 kg which on storage became 4.4 kg, while that formulated with ampicillin sodium increased on storage from 5.3 to > 5.6 kg.

No discoloration or surface crystals of the medicament were observed with all the prepared suppositories on storage for 240 days.

The amount of ampicillin retained after 2 hrs, of dissolution, in suppositories formulated with different bases when fresh and after different time intervals of storage (80,145, and 240 days) are indicated in Table 2 with their K, $t_{1/2}$, and t_{90}.

This table, show that, in general ampicillin sodium was less retained than anhydrous ampicillin indicating its higher stability. The $t_{1/2}$ of ampicillin sodium / Witepsol H_{15} suppositories was 253.5 days, while that of anhydrous ampicillin in the same base was 86 days, while in Novata BD their $t_{1/2}$ were 270 and 65 days respectively. With

respect to the rate and extent of release, this table show that ampicillin sodium was highly retained in polyethylene glycol base. Only 23 %of the medicament released after 2 hrs. In case of ampicillin sodium, the % release were 54 , 63, and 65 in Witepsol H_{15}, Witepsol H_{15} containing 0.1 % polysorbate 80 and Novata BD respectively. This show that ampicillin sodium is less released from polyethylene glycol base than from the two oleaginous bases , Witepsol H_{15} and Novata BD , even in presence of polysorbate 80 in Witepsol H_{15} . As a conclusion of this study , it seems that Witepsol H_{15} cotaining polysorbate 80 and Novata BD bases are the best bases to be medicated with ampicillin sodium.

REFERENCES

1. G. N. , Levy , V. John and J. K. Edward ; J. Pharm. Sci., 63, 1197 (1974).
2. J. K. Edward and G. N. Levy ; J. Pharm. Sci., 61, 727 (1972).
3. J. P. Hou and J. W. Poole ; J. Pharm. Sci., 58, 447 (1969).
4. E. F. Raffanti Jr. and J. C. King ; Am. J. Hosp. Pharm., 31, 745 (1974).
5. D. R. Savello and R. F. Shangraw ; Am. J. Hosp. Pharm., 28 ,754 (1971).
6. I.Setinkar and S. Frntelli ; J. Pharm. Sci., 52, 38 (1963).
7. "The United States Pharmacopeia" , 20 th reu. United States Pharmacopeial Convention , Rockville , MD , 1980, p.959.
8. J. W. G. Smith , G. E. de Grey and V. J. Patel ; Analyst, 92, 247 (1967).