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INVESTIGATIONS ON THE COMMERCIAL ACETAMINOPHEN SUPPOSITORIES IN TURKEY

TÜRKİYEDE ÜRETİLEN ASETAMİNOFEN SUPOZİTUVARLARI ÜZERİNDE ARAŞTIRMALAR

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Acetaminophen that is an analgesic and antipyretic drug is widely being used. It is available in the dosage forms of tablet, syrup, elixir and suppository in Turkish drug market. The suppository dosage form is especially preferred by pediatric and geriatric clinics.

In this study, seven different acetaminophen suppository batches of four different companies obtained from Turkish drug market were investigated. For this purpose the uniformity of weight and content, hardness, disintegration time and dissolution rate of the samples were investigated. The dissolution experiments were carried out according to the USP XXII basket method in the pH 7.2 phosphate buffer solution. The results were evaluated according to the related monograhs of USP XXII and BP 1993.

According to our results, one of the seven commercial acetaminophen suppositories in the market was found not to be in compliance with the USP XXII on drug content. When the dissolution of data of the samples was compared, only one could release 100% of the suppository content at the end of the 45 minutes. Three of them released the active substance among 90-100%; on the contrary the other three samples remained under 75% at the end of the 90 minutes.

Keywords: *Acetaminophen; Suppository; Quality control.*

Analjezik ve antipiretik bir etken madde olan asetaminofen, günümüzde yaygın olarak kullanılmaktadır. Türk ilaç piyasasında tablet, şurup, eliksir ve supozituvar gibi değişik dozaj şekilleri bulunmaktadır. Supozituvar dozaj şekli özellikle pediatride ve geriatride tercih edilmektedir.

Bu amaçla, Türk ilaç piyasasında bulunan dört farklı firmaya ait asetaminofen içeren yedi supozituvar müstahzarı üzerinde çalışılmıştır.

Supozituvar örneklerinde ağırlık sapması, sertlik, erime dağılma zamanı, etken madde miktar tayini ve çözünme hızı tayinleri yapılmıştır. Sonuçlar USP XXII ve BP 1993'e göre değerlendirilmiştir.

Bizim sonuçlarımıza göre, piyasada bulunan 7 asetaminofen supozituvarlarından bir tanesinin ilaç iceriginde USP XXII'ye uygun olmadığı bulunmuştur. Dissolusyon verileri karşılaştırıldığı zaman, yalnızca biri 45 dakikanın sonunda supozituvar içeriğinin %100'ü salınıveriliyor. 3 tanesinde aktif maddenin %90-100'ü salıverildi; diğer üç örnekte ise 90 dakikanın sonunda %75 in altında çözünmeden kalmıştır.

Anahtar kelimeler: *Asetaminofen; Supozituvar; Kalite kontrolu.*

Introduction

Acetaminophen is being widely used as an analgesic and antipyretic drug (1-3). It is available in the dosage forms of tablet, syrup, elixir and suppository in Turkish drug market (4). The suppository dosage form is especially preferred by pediatric and geriatric clinics.

The aim of this study was to investigate the quality controls of suppositories and to determine the compliance of them to the pharmacopoeias and to obtain the dissolution profiles.

Materials and Methods

In this study, seven different acetaminophen suppository batches of four different manufacturers obtained from Turkish drug market were investigated. Their codes and active substance contents are shown in Table 1. Reagents used in the tests were of analytical grade.

The following tests were applied on the suppositories; Uniformity of weight, uniformity of content, disintegration, breaking (hardness) and release studies.

Table 1. Codes and active substance contents of the suppositories.

Code	Active substance content (Acetaminophen in mg)
AC-T	100
AC-S1	100
AC-S2	200
AC-S3	350
AC-PS	120
AC-PF	240
AC-D	325

1- *Evaluation of physical properties of suppositories:*

Uniformity of weight, uniformity of content and disintegration tests were applied according to the BP 1993 (5). The mechanical strength test was carried out on an Erweka breaking strength tester.

2- *Release of acetaminophen from suppositories:*

In vitro release tests were carried out according to the USP XXII basket method (6). The USP rotating basket dissolution apparatus was used for the determination of release rates of acetaminophen from different suppository batches. Each suppository was placed in the basket and lowered into a flask containing 500 ml of phosphate buffer solution (pH 7.2). The basket was rotated at 50 rpm at a constant temperature (37 0.5 °C). 2 ml samples were withdrawn at appropriate time intervals and after dilution with phosphate buffer solution (pH 7.2) acetaminophen was assayed to obtain a dissolution profile. 2 ml phosphate buffer was immediately added to the dissolution medium to compensate for sampling. Released acetaminophen was assayed spectrophotometrically at 242 nm with Pye-Unicam SP 1025 spectrophotometer.

The release data obtained were evaluated kinetically using a computer program written for this purpose (7).

Results and Discussion

1-*Physical characteristics of suppositories:*

All tested suppositories were found to be in compliance with BP 1993 and literature on weight variations, disintegration times and breaking values (5,8).

Except only one suppository coded AC-PS, all suppositories were found to be in compliance with the USP XXII on drug content. The results are given in Table 2.

2- *Release of acetaminophen from suppositories in-vitro*:

The results obtained from the release studies are shown in Figure 1 and Table 3. According to the release rate data given in Fig. 1, the sample coded AC-T releases 100 % of its active substance in 45 minutes. The samples coded AC-S3, AC-PF and AC-D released 87, 91 and 100% of the active substances respectively. However the samples coded AC-S1, AC-S2 and AC-PS released not more than 75 % of their active substance cotent in 90 minutes.

The results of the kinetic assessment of the release data obtained for acetaminophen suppositories are listed in Table 3.

The kinetic assessment of release data showed that the best fit was obtained with Hixson-Crowell kinetic except for AC-PS and AC-D coded suppositories. However the best fit was obtained with first order and zero order kinetics respectively for AC-PS and AC-D coded suppositories.

Table 2. Weight variation, content uniformity, breaking value and disintegration time of suppositories.

Codes	Weight variation (g)		Content uniformity (mg)		Breaking value (kg)		Disintegration time (min)	
	X	±SD	X	±SD	X	±SD	X	±SD
AC-T	0.96	5.25	100	4	3.87	0.74	5.90	0.86
AC-S1	0.96	0.01	91.9	3.3	>6.80	—	6.25	0.29
AC-S2	1.22	4.10	207	3	>6.80	—	8.1	0.7
AC-S3	1.72	9.05	337	10	>6.80	—	8.8	1.9
AC-PS	0.97	0.02	94	7	1.68	0.13	3.59	0.15
AC-PF	1.98	0.01	234	3	3.16	0.35	8.35	0.32
AC-D	1.00	1.76	329	3	3.86	0.06	7.68	0.52

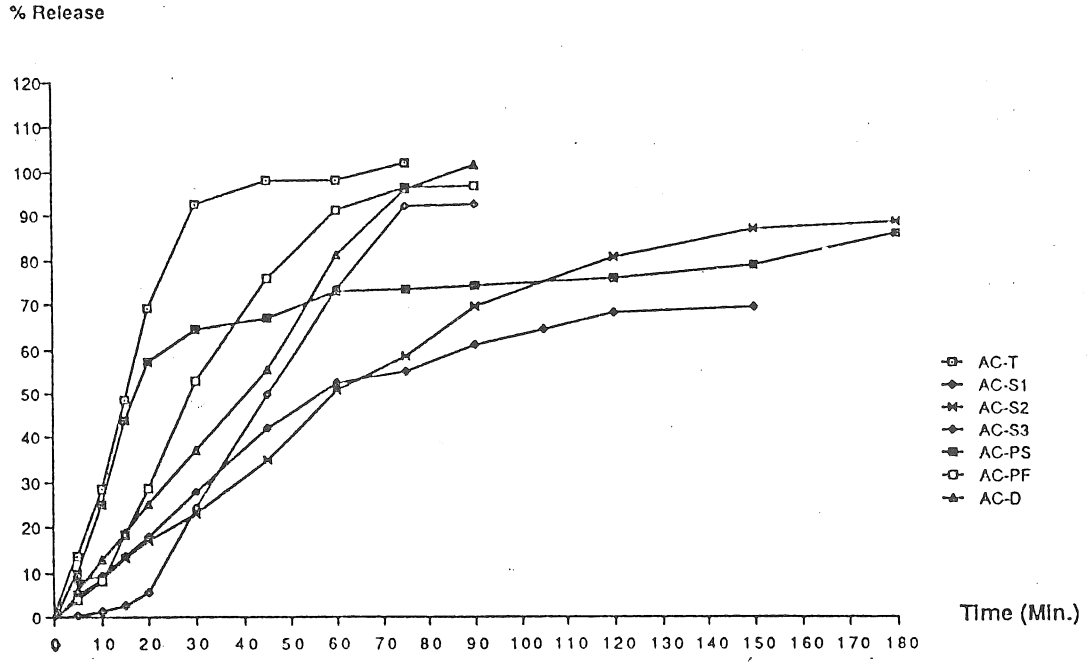

Figure 1. The release profiles of acetaminophen from the suppositories.

Table 3. The kinetic assessment of release data

KINETICS		AC-T	AC-S1	AC-S2	AC-S3	AC-PS	AC-PF	AC-D
O°	kr°	70.4	28.7	63.4	221	22.4	176	233
	r	0.732	0.898	0.931	0.919	0.602	0.913	0.984
	SSD	0.494	0.151	0.129	0.141	0.122	0.114	0.183
	SWSD	0.509	0.285	-0.323	0.365	0.169	-0.143	-0.359
1°	kr	11.7	0.52	0.802	6.67	0.504	2.75	8.43
	r	0.718	0.954	0.989	0.625	0.804	0.981	0.565
	SSD	0.864	0.433	0.34	0.277	0.872	0.367	0.216
	SWSD	0.48	0.775	0.618	0.259	0.128	0.907	0.366
Hixson-Crowell	K	2.41	0.465	0.698	1.84	0.619	1.9	2.23
	r	0.941	0.937	0.98	0.96	0.739	0.978	0.33
	SSD	0.308	0.433	0.936	0.317	0.576	0.706	0.184
	SWSD	0.162	0.972	0.397	0.595	0.988	0.131	0.539

kr^0 : Zero order release rate constant ($mg.h^{-1}$).
kr : First order release rate constant (h^{-1}).
K: Dissolution rate constant calculated from the Hixon-Crowell Plot for sink conditions.
r^2: Determination coefficient.
SSD: Sum of squared deviations.
SWSD: Sum of weighted squared deviations.

References

1. The Pharmaceutical Codex, 11th Ed., The Pharmaceutical Press, London, 1979
2. Kayaalp, S.O. (Ed) : Rasyonel Tedavi Yönünden Tıbbi Farmakoloji, Cilt 2, Feryal Matbaası, Ankara, 1990
3. Drwal-Klein, L.A., Phelps, S.J.: Clin. Pharm. 11, 1005 (1992)
4. Ommaty, R. (Ed): Vademecum 94, Modern İlaç Rehberi, Ankara, 1994
5. British Pharmacopoeia 1993, Vol II, University Printing House, Cambridge, England
6. USP XXII, United States Pharmacopoeia, Conv. Inc. 2601, Twinbrook Parkway Rockville MD 20852, 1990
7. Ağabeyoğlu, I.T.: 'DISSOL', XVIII e, Semaine Médicale Balkanique Abstracts, p.327 İstanbul, 30 August-4 September 1984
8. Lachman, L., Lieberman, H.A., Kaning, L.L. (Eds): The Theory and Practice of Industrial Pharmacy, 3rd ed., Lea and Febiger, Philadelphia 1986

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