FABAD Farm. Bil. Der.
12, 289 - 295, 1987

FABAD J. Pharm. Sci
12, 289 - 295, 1987

Investigation Of Stability Of The Pharmaceutical Colorants Exposed To Sunlight

Nilüfer TARIMCI (*)
İlbeyi AĞABEYOĞLU (**)
Nurşin GÖNÜL (*)
Tamer BAYKARA (*)

Summary : In this study, the stability kinetics of ten certified dyes used in food, drug and cosmetics in Turkey were investigated in distilled water exposed to sunlight.

For this purpose, the fading values of the dye solutions were determined at defined time intervals and the data were evaluated kinetically using computer programmes.

The results showed good fits for two dyes to zero order kinetics, and for the remaining eight dyes to the first order kinetics equation, respectively.

FARMASÖTİK BOYAR MADDELERİN IŞIĞA KARŞI STABİLİTELERİNİN İNCELENMESİ

Özet : Bu çalışmada, farmasötik endüstride kullanılmasına izin verilen on adet boyar maddesinin sulu ortamda ışık etkisi altındaki stabilite kinetikleri incelenmiştir.

Bu amaçla, hazırlanan boya çözeltilerinin belli zaman aralıklarında solma değerleri saptanmış ve verilen bilgisayar programları kullanılarak kinetik açıdan değerlendirilmiştir.

(*) Ankara Üniversitesi Eczacılık Fakültesi Formasötik Teknoloji Anabilim Dalı.

(**) Gazi Üniversitesi Ecz. Fak., Farmasötik Teknoloji Anabilim Dalı.

Elde edilen sonuçlara göre, iki boyanın sıfır derece kinetiğe, sekiz boyanın da birinci derece kinetiğe daha iyi uyum gösterdikleri gözlenmiştir.

Keywords : Pharmaceutical colorants, stability, kinetic evaluation.

INTRODUCTION

In pharmaceutical industry, coloring the pharmaceutical preparations for some purpose such as eye appeal, masking, identification and patient acceptance is a frequent pharmaceutical practice (1).

When a pharmaceutical preparation has been colored for the above mentioned purposes, such coloring should be maintained till the product has been consumed by the consumer, who may associate color maintenance with potency maintenance of the product. Therefore, a most important legal and moral obligation of the ethical pharmaceutical foundations, such as drug factories and laboratories, which produce pharmaceutical preparations, is to market their product that should maintain their label potencies and initial appearance for the duration of market or sfelflife (1, 2).

The certified drug and cosmetic dyes are used as colorants in pharmaceutical preparations (3-5).

Colorants have some problems as in other pharmaceutical additives (6-9). The most important of these is their own stability. In pharmaceutical preparations, they fade because of the effect of various factors and lose the purpose of their employment (10).

In a previous study (11), the effect of light intensity and the pHs of the media were investigated on the color stability of F.D.C. dyes and the degradation percentages in relation to their degradation kinet were determined.

In this study, the stability of ten certified dyes used in pharmaceutical industry in Turkey were investigated in distilled water exposed to sunlight and the order of their degradation reactions were determined.

THEORETICAL

Prediction of the stability of drugs and pharmaceutical preparations are based on data obtained from experimental results and the stability of drugs are expressed by quantitative mathematical expressions (11).

The dyes which are exposed to sunlight in different media and conditions, are degraded by zero and first order kinetic equations (12).

The following equations are used in degradation by zero or first order kinetic reactions (1, 13, 14

a. Zero-order equation :

$$A = A_o - k_o t$$

b. $\ln A = \ln A_0 - kt$

c. First-order equation with an asymptotic value :

$$\ln (A - A\infty) = \ln (A_0 - A\infty) - kt$$

Where,

A_o : Absorbance at time zero

A : Absorbance at time t

$A\infty$: Absorbance at time $t = \infty$

k_o, k : Rate constants for zero and first - order respectively.

t : time

MATERIALS AND METHODS :

The dyes used in the study are in monoazo and diazo classes from the chemical structure aspect, and they are certified dyes for the food, drug and cosmetic preparations. They are given in (Table 1). 0.001 % w/v aqueous solutions of each dye were prepared and exposed to sunlight for approximately 80 days. During that time, the absorbances were determined at certain time intervals (10).

Table 1. Dyes used in the study

Test Number		Number Color Index
2	Food Orange 2, Orange GGN, C-Orange 9	15980
3	F.D.C. Yellow N. 6, Sunset Yellow FCF	15985
4	Food Red 2, Scarlet GN	14815
5	FDC Yellow No. 5, Tartrazin	19140
6	Food Red 3, Azorubin	14720
7	Fast Red E, Genuine Red E	16045
8	F.D.C. Red No : 2, Amaranth	16185
9	Food Red 7, Cochineal Red	16255
10	Food Red 8, Acid Red 41	16290
13	Food Black 1, Brilliant Black BN	28440

The data obtained were fit to kinetic model equations by the method of least squares employing a computer programme written for this purpose (15). After this, the parameters obtained were op-

Table 2. The Kinetic Assessment of Data.

Test Number	Zero Order			First Order			First Order with asymptotic value				First Order Nonlinear Regression			
	k_o	A_o	r^2	k_o	A_o	r^2	k	A_o	$A\infty$	r^2	k	A_o	$A\infty$	r^2
2	0.00174	0.446	0.943	0.00466	0.449	0.947					0.00472	0.451		0.952
3	0.00191	0.551	0.934	0.00398	0.553	0.952					0.00413	0.556		0.954
4	0.00205	0.348	0.974	0.00791	0.357	0.970					0.00781	0.356		0.977
5	0.000839	0.397	0.948	0.00233	0.398	0.943					0.00231	0.398		0.946
6	0.00232	0.557	0.816	0.00490	0.559	0.824	0.0451	0.611	0.400	0.997	0.0371	0.157	0.381	0.963
7	0.00192	0.445	0.958	0.00528	0.449	0.965					0.00533	0.449		0.965
8	0.00245	0.524	0.936	0.00568	0.527	0.952					0.00595	0.533		0.961
9	0.00182	0.430	0.945	0.00505	0.434	0.965					0.00522	0.436		0.961
10	0.00262	0.406	0.926	0.00505	0.434	0.965	0.0379	0.459	0.220	0.977	0.0459	0.459	0.217	0.849
13	0.00216	0.533	0.951	0.00482	0.536	0.969					0.00499	0.540		0.976

k_o : Zero order rate constant (Absorbance . day^{-1})
k : First order rate constant (day^{-1})
A_o : Initial absorbance
$A\infty$: Asymptotic value of the absorbance
r^2 : Determination coefficient

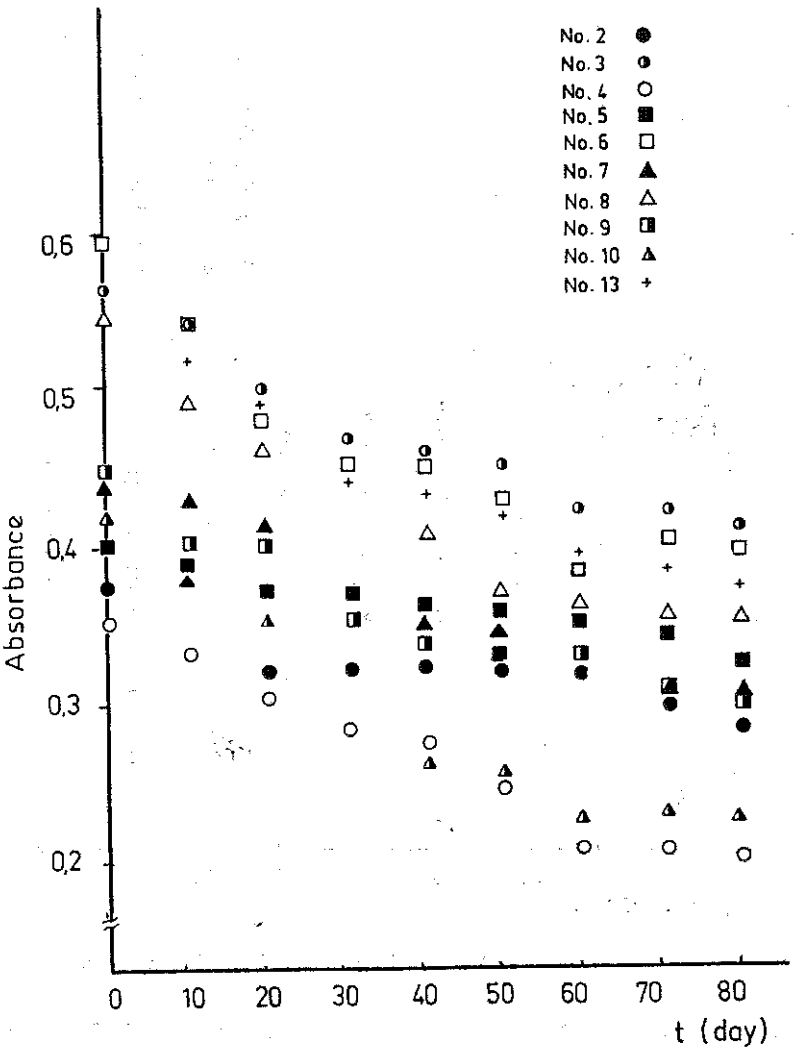

Fig 1. Linear degradation profiles of the dyes.

timized to the data by a nonlinear regression program employing Bard algoritm (16).

Results and Discussion:

The linear and semi-log plots of absorbances vs. time are giv- in Figs 1 and 2.

The kinetic assessment of the data are given in Table 2.

The majority of the dyes appear to degrade by first order kinetics Zero order kinetics seems to better describe the degradation of two dyes (Scarlet GN, Tartrazin).

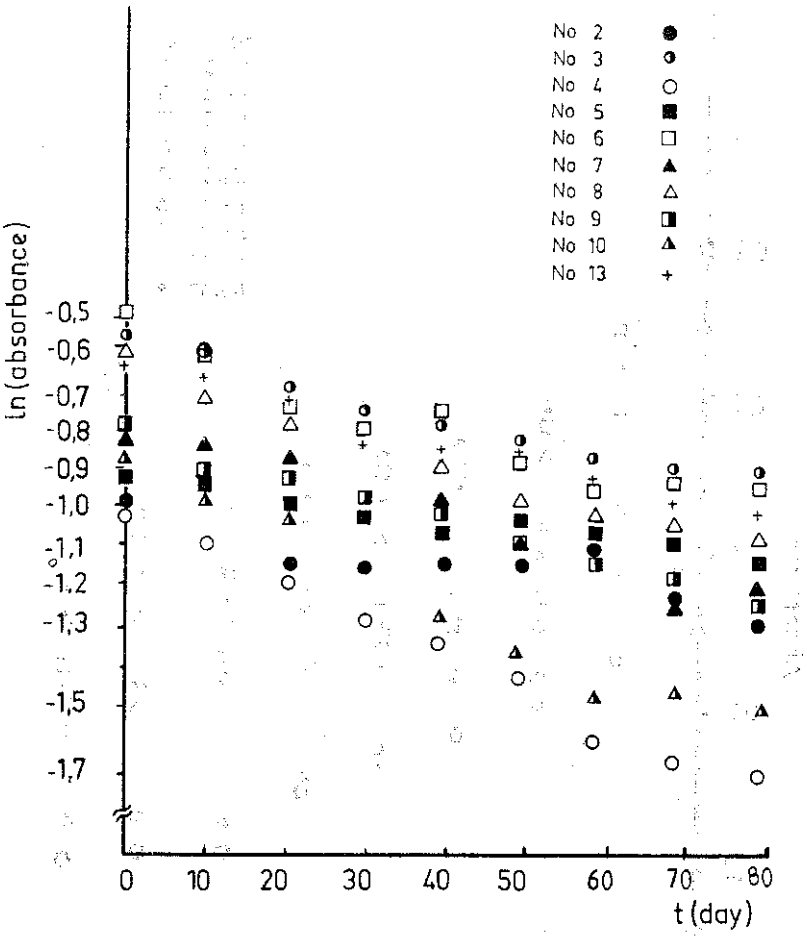

Fig 2. Semilogaritmic degradation profiles of the dyes.

Since two of the dyes (Azorubin and Acid Red 41) have an asymptotic absorbance, the equation with an A term is better suited for kinetic assessment.

In this work, we found that nonlinear regression did not improve the parameter values to a great extent.

REFERENCES

1 — Garret, E. R., Carper, R. F. «Prediction of Stability in Pharmaceutical Preparations I. Color Stability in a Liquid Multisulfa Preparation», J. Am. Pharm. Assoc., 44, 515-518, 1955.

2 — Parrot, E.L. : Flavor and Color, Experimental Parmaceutics, Burgess Publishing Company, U.S.A., 4th Ed., p. 120 1977.

3 — Scherer. Rp. GmbH, Eber bach-Baden : Stand July 1966.

4 — «Regulations on the 188th article of the General Hygiene Law, No : 1503», Turk. Rep., Ministry of Health and Social Assistance, Pub. No : 144, Ankara 1962.

5 — «Cosmetic Regulation», ibid., Pub. No : 339, Ankara 1979.

6 — Hess, H., Schrank, J., «Colouration of Pharmaceuticals-Possibilities and Technical Problems», Acta Pharm. Technol., 25, 77-87 (Suppl. 8), 1979

7 — Juhlin, L., «Intolerance to Dyes Used in Drugs», Acta Pharm. Techn. 25, 15-19 (Supp. 8). 1979.

8 — Brownley, C.A., JR., Lachman, L., «Preliminary Report on the Comparative Stability of Certified Colorants With Lactose in Aqueous Solution», J. Pharm. Sci., 52, 86-93, 1963.

9 — Millstone, E. : New Scientist, No. 1426, s. 20-24, 1984.

10 — Lachman, L. and de Luca, P., «Kinetic Principles and Stability Testing», Lachman, L. Lieberman, H.A and Kanig, J.L., «The Theory and Practice of Industrial Pharmacy», 2. Ed., Lea and Febiger, Philadelphia, p. 55-56. 1976.

11 — Czetsch-Lindenwald, H., Gönül, N., «Stabilities of Dyes in Different Media Under the Effect of the Light», J. Fac Pharm. Ankara, 2, 11, 1972.

12 — Garrett, E.R., «Prediction of Stability of Drugs and Pharmaceutical Preparations», J Pharm. Sci., 51, 811-833, 1962

13 — Goodhart, F.W., Everhard, M.E., Dickcius, D A., «Stability of Certified Dyes in Tablet II. Fading of FD-C Red No. 3 and FDC Red No. 3 Aluminum Lake in Three Tablet Formulas», J. Pharm. Sci., 53 338-340, 1964.

14 — Martin, A., Swarbrick, J and Cammarata, A., «Physical Pharmacy, Physical Chemical Principles in Pharmaceutical Sciences», Lea and Febiger, 3 rd Ed., p. 352-398, 1983.

15 — Ağabeyoğlu, İ.T. : EKAR18, ILB, University of Ankara, Faculty of Pharmacy, Computing Center, Ankara 1982.

16 — Anon., «Nonlinear Parameter Enstimation and Programming», in «Catalog of Programs for IBM System 360 Models 25 and Above», GC 20-1619-8; Prog. No. 360 D-13.6.003, P. 237.