

STABILITY OF ASPIRIN-ARGININE AND ASPIRIN-LYSINE SALTS

ASPIRİN-ARGİNİN VE ASPIRİN-LİZİN TUZLARININ STABİLİTESİ

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*The stability of aspirin-arginine, aspirin-arginine-glycine and aspirin-lysine salts in aqueous medium were investigated at room temperature and refrigerator (4°C). They were found to be stable in the refrigerator for 24 hs whereas at room temperature they must immediately be consumed.*

*Aspirin-arginin, aspirin-arginin-glisin ve aspirin-lizin tuzlarının sulu vasatta oda temperaturünde ve 4°C de stabilitesi incelenmiştir. Buzdolabında her 3 denenen aspirin tuzunda stabilitesinin 1 gün olduğu saptanmıştır. Oda temperaturünde ise bekletilmeden kullanılması tesbit edilmiştir.*

**Keywords:** Aspirin-arginine; Aspirin-lysine; Stability test

**Anahtar kelimeler:** Aspirin-arginin; Aspirin-lizin; Stabilite testi

## Introduction

Aspirin is not soluble in water whereas its amino acid salts as arginine (1-4), lysine (1, 4-8), histidine (1, 4) and ornithine (9) are soluble. Of these only aspirin-lysine salt is used for injection in medicine (8).

Aqueous solution of aspirin-arginine salt containing glycine was heated for 16 h and found that it was hydrolysed to salicylic acid 50-60% (3). In the stability tests of aspirin-lysine solution it was found that the aspirin remained after 4 days was 55% at room temperature and 90% at 2°C (10).

In this work, the stability of aqueous solutions was studied of aspirin-arginine (I), aspirin-arginine plus glycine (II) and aspirin-lysine (Aspisol) (III). The losses of aspirin were determined depending on its hydrolyzed product i.e. salicylic acid (11).

## Material

Aspirin-arginine salt(12). Aspisol (Bayer), aspirin (Bayer), arginine (Fluka). All chemicals were Merck products.

## Method

### Preparation of aspirin-arginine salt (12)

1 g aspirin was dissolved in a mixture of 1 ml methanol-9 ml diethyl ether then mixed with 0.96 g arginine in 6.5 ml ethanol (90%), shaken for 2 min. The water phase was poured into acetone. The semisolid part was separated and washed five times with acetone and filtered under vacuum. Its purity was controlled by tlc. (Adsorbent:

silicagel G 60 (Merck). Solvent system: hexane-acetic acid-chloroform (85:15:10), Reagents : I-Ferric nitrate; 1% in 0.1 % nitric acid, II-Ninhydrine; 0.2% in ethanol)

### Aspirin assay

Aspirin amount was determined on hydrolysis product of salicylic acid (11).

### 1-Salicylic acid determination

0.250 g Salicylic acid was dissolved in 7.5 ml ethanol (95%) and the volume was adjusted to 500 ml with distilled water. 10 ml was taken and adjusted to 100 ml with distilled water. 2.5-20 ml from this solution (50 mcg ml<sup>-1</sup> of salicylic acid) was added to 5 ml of 1% ferric nitrate solution and the volume adjusted to 25 ml with distilled water. The absorbance was read in a spectrophotometer (Shimadzu Double-Beam UV 150 02) at 525 nm. The standard curve was plotted and its equation was calculated.

### 2- Aspirin assay in tested salts

100 mg of tested salts, 2.5 ml potassium hydroxide (10%) solution in 2.5 ml ethanol (95%) were placed in a flask and heated under reflux for 2 h in a water bath, then cooled. It was acidified with 0.5 ml conc. HCl and the volume was adjusted to 50 ml with distilled water. 0.4 ml was taken and 1 ml ferric nitrate (1%) solution added, then the volume adjusted to 10 ml with distilled water. Absorbance was read against a blank at 525 nm. Salicylic acid amount was found from the equation and hence the aspirin amount calculated.

### Stability test

Preparation of tested solutions: (I) 50 mg aspirin-arginine salt was dissolved in 25 ml distilled water. (II)

50 mg aspirin-arginine salt and 0.005 g glycine were dissolved in 25 ml distilled water. (III) 50 mg Aspisol was dissolved in 25 ml distilled water.

All the solutions were prepared in 5 ml siliconized flacons capped with rubber and stored at room temperature or refrigerator. The amount of salicylic acid was determined daily for 10 days at room temperature and 29 days in refrigerator. The hydrolysed product of salicylic acid was determined daily and therefrom the aspirin amount calculated.

## Results and Discussion

The equation of the standard curve for salicylic acid was found as:  $y=0.0124x-0.0079$ ,  $r:0.999$ .

The amount of aspirin before and after in the tests was calculated in its salts I, II and III by means of the above equation.

The percentages of aspirin in (I): found; 47.05 mg, calc. 47.2 mg ( $C_{15}H_{22}N_4O_6 \cdot 1/2 H_2O$ ), in Aspisol: found 49.93 mg, calc. 50 mg. The compound I and Aspisol showed one spot on tlc. The stability results of the tested salts are shown in the Table.

Table : Percentage of aspirin remained

Day	I		II		III	
	R.T.	Refrig.	R.T.	Refrig.	R.T.	Refrig.
1	81.23	90.76	86.68	93.76	82.83	92.06
2	73.06	83.68	76.33	88.82	71.02	86.42
3	65.70	79.87	63.80	85.59	64.08	83.34
4	62.44	76.60	59.71	83.41	55.61	81.54

R.T.: Room temperature, Refrig.: Refrigerator, I: Aspirin-arginine, II: Aspirin-arginine plus glycine, III: Aspirin-lysine

At room temperature the aspirin remained (%) were 24.57 for (I), 29.74 for (II) and 19.15 for (III) after 10 days. In refrigerator the corresponding values were 57.29 for (I), 66.79 for (II) and 67.67 for (III) after 10 days and 37.92 for (I), 40.64 for (II) and 40.20 for (III) after 29 days.  $t_{90}$  values at room temperature; 20 h for (I), 23 h for (II) and 18 h for (III) and in refrigerator; 31 h for (I), 32 h for (II) and

3 h for (III). The stability of aspirin-arginine salt and aspirin lysine salt (Aspisol) gave similar results. Hence both must be used within 24 h.

Our findings on the stability of aspirin-lysine salt agree with the findings of Miyake et al. (10) at room temperature but in refrigerator we found 33 h at 4°C against 4 day at 2°C.

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