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Chromatographic Behaviour of Antibiotics on Thin Layers of Zeolite

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Introduction: Antibiotics analysis is performed by many methods such as spectrophotometry, fluorimetry, polarography, and high-performance liquid chromatography. This analysis doesn't require derivatization but requires expensive equipment and extensive preparation. When more than one antibiotic is present in a formulation, interactions may occur between the drugs that must be separated before measurement. Thin-layer chromatography is a useful technique for identifying antibiotics because of the low cost, high speed, and low servicing. Silica gel adsorbents have often been used as adsorbents in all thin-layer chromatography studies. In this study, zeolite was used as an adsorbent in thin- layer chromatography with high selectivity.

Materials and Methods: The chromatographic behaviour of amoxicillin, ampicillin, cefazolin, cefixime, ceftriaxone, cefalexin, and penicillin was studied for the first time on a thin layer of zeolite with mobile, organic, and organic- organic phases.

Discussion: The best separation of ceftriaxone from amoxicillin, ampicillin, cefazolin, cefixolin, cefalexin, and penicillin on a thin layer of zeolite using methanol as the mobile phase. The distance and rise time are 12 cm and 110 minutes, respectively.

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Conclusion: The results of the present study showed that using the current method, the selectivity of one antibiotic from other components as well as two-component andthree-component adsorption was obtained. Quantitative identification of antibiotics was also performed in multicomponent mixtures after selection of appropriate isolates.

Keywords: Zeolite adsorbent; thin-layer chromatography; antibiotics; chromatographic behaviour.

1. INTRODUCTION

Analysis of antibiotics has been performed by many methods, e.g. spectrophotometry [1,2], fluorimetry [3,4], polarography [5,6] and high-performance liquid chromatography (HPLC), which requires not only derivatization but also expensive equipment and extensive sample preparation [7,8]. When more than one antibiotic is present in a formulation, interaction between the antibiotics can occur [9] which necessitates their separation before determination. Thin-layer chromatography is one of the most important analytical techniques used to separate components of mixtures. TLC is often used as a quick, easy and simple method [10-16]. The effective separation by the depends on the properties of the sample, and those of the mobile and stationary phases [17-18]. Several materials hare previously been used as TLC adsorbents activated bentonite [19], activated bleaching earth [20], china day [21]. Silica gel and alumina have been most frequently as adsorbents for separation to the components of the mixtures in TLC application On TLC adsorbent materials should be inexpensive and easily available. Zeolite as a major component of detergent. This paper reports the retention behaviour of seven common antibiotics on thin layers of the zeolite 4A. Some selective methods have been developed for separation of one antibiotic from others in a single-step process. Important multiple separations of the antibiotics have also been achieved.

2. Experimental

2.1 Chemical and Reagents

All reagents were of analytical grade (Merck). The reagents used are listed in Table 1.

The antibiotics studied were Amoxicillin, Ampicillin, Cefazoline, Cefixime, Ceftriaxone, Cephalexin and Penicillin. All of the standards were 0.05 molar that obtained with distilled water.

2.2 Solvent Systems

The compositions of the solvent system used are listed in Table 2. Detection was performed by exposing the plates to Iodine vapour.

2.3 Apparatus

Camag automatic TLC plate coater, Glass plates 20*20 cm, Chromatographic chambers, UV lamp, Sprayer, Cabinet sprayer.

2.4 Preparation of Plates

70 g of zeolite is added gradually to 70 ml of water and then 4 g of silica gel is added it when made a gel 1 g of silica gel 60 g is added. As the binder, in a conical flask with Teflon stopper, and shaking the flask vigorously for 3 min. The slurry was then poured immediately into a Camag automatic TLC plate coater and use to

Table 1. List of reagents

Reagent Standard	Iodine vapour	1% Ninhydrin in Ethanol	H_2SO_4 conc.	5% $K_2Cr_2O_7$ in H_2SO_4	Vanillin In Ethanol
Amoxicillin	Yellow	*	Black	White-Blue	*
Ampicillin	Yellow	Pink	Black	White-Blue	*
Cefazoline	Yellow	*	Black	White-Blue	*
Cefixime	Yellow	*	Black	White-Blue	*
Ceftriaxone	Yellow	Pink	Black	White-Blue	*
Cephalexin	Yellow	Pink	Black	White-Blue	*
Penicillin	Yellow	*	Black	White-Blue	*

** Non detected*

Table 2. List of solvent systems

No.	Solvent systems	No.	Solvent systems
1	Acetic acid 1 M	12	Buffer- acetonitrile (85:15)
2	Acetone	11	Buffer- methanol (85:15)
3	Acetonitrile	12	Chloroform-acetic acid (30-1)
4	Ammonium chloride	12	Cyclohexane-chloroform (2-8)
5	Ammonia 25%	12	Formic acid-acetone (5-3)
6	Chloroform	12	Methanol-water(1-1)
7	Dimethylformamide	12	Methanol-benzene (5-1)
8	Dioxane	12	Methanol-sodium chloride%5(2-1)
9	Ethanol	12	Methyl ethyl ketone-acetic acid (4-1)
10	Ethyl acetate	23	Chloroform-Methanol-Tri ethylamine (90-10-5)
11	Heptane	22	Ethyl acetate- 1- propanol- water(3:5:3)
12	Hexane	21	Ethyl acetate-methanol-NH4OH(%25)(85-10-5)
13	Methanol	22	Ethylacetate-Methanol-Ttri ethylamine (43-5-2.5)
14	Methyl ethyl ketone	22	Ethyl acetate –Methanol-Tri ethylamine (43-25-2.5)
15	n-Butanol	22	n-butanol- acetic acid-water(5:4:2)
16	n-Propanol	22	n-butanol- acetic acid-water(20:2:1)
17	Toluene	22	Toluene-ethylacetate-Ttriethyle amine (7-2-1)
18	Vinyl acetate	22	Ethanol-pyridine- dioxane-water (50-20-25-5)
19	Water(demineralized)	22	Toluene-Acetone-Methanol-NH4OH(%25)(20-20-3-1)
20	Buffer*- acetone (85:15)	23	Chloroform-Methanol-Tri ethylamine (90-10-5)

coat eight 20 cm[1] 20 cm glass plates with a 300-micrometre layer. The plate was dried in an oven at 60 centigrade for 2 h then stored at room temperature.

3. CHROMATOGRAPHY

Antibiotic solutions were applied to the plates as circular spots using disposable fine glass capillaries. The spots were dried completely and the plates were developed in an ascending mode (without conditioning) in a Camag chamber. The development distance was always 12 cm from the origin. After development, the plates were dried in air and the antibiotics were detected with appropriate reagents Iodine vapour was used to locate all of the antibiotics in this investigation.

4. RESULTS AND DISCUSSION

In binary mixtures, after selective separations, quantitative determinations of some antibiotics have been done by instrumental thin layer chromatography as follows:

1. The best separation of Ceftriaxone has been developed from Amoxicillin, Ampicillin, Cefazoline, Cefixime, Cephalexin and Penicillin on thin layers of zeolite using Methanol as a mobile phase. The development distance and time were 12 cm and 110 min respectively.
2. A rapid and selective binary separation of Ampicillin and Cefixime has been developed from five other antibiotics on a thin layer of zeolite using Formic Acid 1 M as a mobile phase. The development distance and time were 12 cm and 45 min respectively.
3. As a ternary separation of has been developed Amoxicillin, Cefazoline, Cefixime from Ampicillin, Ceftriaxone, Cephalexin and Penicillin on a thin layer of zeolite using Ethanol as a mobile phase. The development distance and time were 12 cm and 140 min respectively.

The obtained results during the study of the chromatographic behaviour of antibiotics on the thin layer of zeolite clearly show that the stationary phase zeolite is valid and useful for the separation of antibiotics in thin layer chromatography. The compounds isolated by iodine vapours are detected on the plates, and the results show that in some systems, one or more antibiotics can be separated from the others.

The multiple separation systems in Table 3-4 show the appropriate separations achieved i n

[1] *15% w/v of ammonium acetate adjusted to pH 6.2 with glacial acetic acid.*

most solvent systems. The best mobile phase, which was a combination of butanol: water: acetic acid (5:4:2), was able to separate all seven antibiotics by a slight difference separately. The mobile phase consisted of methyl ethyl ketone: acetic acid other than cefixime and Cefalexin segregates other components. The mobile phases of ethanol, methanol, and ethanol mixtures: Pyridine: Dioxane: Acetic acid were able to separate four elements, three ingredients, and two components from seven parts, respectively. It should be noted that the selectivity of the dissociation in the zeolite system was better than the silica gel plates in the investigated systems. It is also suggested for future research that: In the pharmaceutical industry: Due to the good results obtained from zeolite adsorbent as a stationary phase in thin-layer chromatography, it is possible to extend the studies in the drugs sector and to collect the chromatographic behaviour guide of all the drugs on this phase and to plot it. Specialist chromatography manufactures a thin layer of zeolite, such as silica gel plates, and uses the quantitative measurement of pharmaceutical mixtures in the pharmaceutical industry, which can produce lower prices and more effective results. In laboratories: Since zeolites are only compatible with cations, the available cations can be identified and measured by zeolite plates.

Table 3. Separation of one antibiotic from other antibiotics on thin layers of Zeolite 4A

Separation ($hR_T - hR_L$)	Mobile phase	Interference	Time (min)
Amoxicillin(43-50) From 6 antibiotic compounds		-	
Ampicillin(34-40) From 6 antibiotic compounds		-	
Cefazoline(26-32) From 6 antibiotic compounds	n-Butanol- Acetic Acid- Water(5:4:2)	-	
Cefixime(18-22) From 6 antibiotic compounds		-	125
Ceftriaxone(13-16) From 6 antibiotic compounds		-	
Cephalexin(9-12) From 6 antibiotic compounds		-	
Penicillin(4-7) From 6 antibiotic compounds		-	
Cefazoline(73-83) From 6 antibiotic compounds		-	230
Penicillin(0-17) From 6 antibiotic compounds	Acetone	-	60
Ceftriaxone (13-24) From 6 antibiotic compounds		-	145
Cefazoline (95-100) From 6 antibiotic compounds		-	
Amoxicillin(63-69) From 5 antibiotic compounds	Methyl ethyl ketone-acetic acid(4:1)	Cephalexin	145
Penicillin(71-74) From 5 antibiotic compounds		Cefixime-Cephalexin	
Ampicillin(75-82) From 5 antibiotic compounds		Cefixime	145
Cefixime(75-98) From 4 antibiotic compounds		Cephalexin-Penicillin	
Cephalexin (67-73) From 5 antibiotic compounds	Methyl ethyl ketone-acetic Acid (4:1)	Amoxicillin- Cephalexin- Penicillin	
Ceftriaxone (72-78) From 6 antibiotic compounds	Methanol	-	
Ampicillin(91-93) From 4 antibiotic compounds		Amoxicillin-Cefazoline	110

Separation ($hR_T - hR_L$)	Mobile phase	Interference	Time (min)
Cephalexin(85-88) From 4 antibiotic compounds		Ampicillin-Cefixime- Penicillin	
Penicillin(82-87) From 4 antibiotic compounds		Cefixime- Cephaloxin	
Cefazoline(88-93) From 3 antibiotic compounds		Amoxicillin-Cefixime- Penicillin	
Penicillin(61-65) From 6 antibiotic compounds		-	
Ceftriaxone(81-87) From 6 antibiotic compounds		-	
Cefixime(88-93) From 5 antibiotic compounds		Cephalexin	135
Cefazoline(96-100) From 4 antibiotic compounds		Amoxicillin-Ampicillin	
Amoxicillin(95-100) From 4 antibiotic compounds	Dimethylformamide	Cefazoline-Ampicillin	
Ampicillin(97-100) From 3 antibiotic compounds		Amoxicillin-Cefazoline	
Cephalexin(91-96) From 4 antibiotic compounds		Cefixime-Amoxicillin	
Cefazoline(16-21) From 6 antibiotic compounds		-	80
Cefixime (7-12) From 5 antibiotic compounds	Dioxane	Ceftriaxone	
Ceftriaxone(11-15) From 5 antibiotic compounds		Cefixime	
Penicillin(23-29) From 5 antibiotic compounds	Ethanol-Pyridine- Dioxan-Acetic	Cefixime	165
Cefixime(29-51) From 5 antibiotic compounds	acid(50:20:25:5)	Penicillin	
Amoxicillin(5-30) From 4 antibiotic compounds		Lk;	
Cefazoline(4-21) From 4 antibiotic compounds		Amoxicillin-Ceftriaxone	90
Ceftriaxone(3-13) From 4 antibiotic compounds		Amoxicillin-Cefazoline	
Ceftriaxone(67-75) From 5 antibiotic compounds		Cefixime	
Cefixime(70-77) From 4 antibiotic compounds		Ceftriaxone-Penicillin	124
Penicillin(75-84) From 4 antibiotic compounds	Ethyl acetate-acetic acid- water(3:3:1)	Cefixime-Cephalexin	
Amoxicillin(92-99) From 4 antibiotic compounds		Ampicillin-Cefazoline	
Cephalexin(81-92) From 4 antibiotic compounds		Penicillin-Cefazoline	124
Ampicillin(93-99) From 4 antibiotic compounds		Amoxicillin-Cefazoline	
Cefazoline(85-94) From 4 antibiotic compounds		Amoxicillin-Ampicillin	
Ceftriaxone (0-12) From 6 antibiotic compounds		-	
Cefixime (17-26) From 6 antibiotic compounds		-	
Cefazoline (53-58) From 5 antibiotic compounds		Penicillin	140

Separation (hR_T - hR_L)	Mobile phase	Interference	Time (min)
Cephalexin (73-81) From 4 antibiotic compounds	Ethanol	Penicillin-Amoxicillin	
Amoxicillin (79-92) From 4 antibiotic compounds		Penicillin-Ampicillin	
Ampicillin (90-94) From 4 antibiotic compounds		Penicillin-Amoxicillin	
Ampicillin (17-21) From 3 antibiotic compounds		Cefazoline- Ceftriaxone- Cephalexin	
Cefazoline (16-40) From 3 antibiotic compounds	Ethyl Acetate- methanol- Ammonia 25%(85:10:5)	Ampicillin -Ceftriaxone- Cephalexin	90
Ceftriaxone (14-18) From 3 antibiotic compounds		Cefazoline-Ampicillin- Cephalexin	
Cephalexin (16-22) From 3 antibiotic compounds		Cefazoline-Ampicillin- Ceftriaxone	

Table 4. Ternary and binary separations achieved on zeolite 4A plates

Mobile phase	Separation(hR_T - hR_L)	Time (min)
Ethanol	Amoxicillin(80-93)Cefazoline(52-57)Cefixime(18-26) Amoxicillin(79-93)Cefazoline(53-59)Ceftriaxone(0-11) Amoxicillin(80-94)Cefixime(18-26)Ceftriaxone(0-12) Ampicillin(91-94)Cefazoline(52-58)Cephalexin(71-79) Ampicillin(92-95)cefazoline(53-59)Cefixime(16-25) Ampicillin(89-92)Cefazoline(52-57)Ceftriaxone(0-11) Ampicillin(90-93)Cefazoline(53-58)Ceftriaxone(0-12) Ampicillin(91-95)Cefixime(17-25)Ceftriaxone(0-13) Ampicillin(92-96)Cefixime(18-26)Cephalexin(71-80) Ampicillin(90-93)Ceftriaxone(0-12)Cephalexin(72-79) Cefazoline(52-58)Cefixime(17-26)Ceftriaxone(0-12) Cefazoline(53-59)Cefixime(17-27)Cephalexin(71-78) Cefazoline(52-57)Ceftriaxone(0-11)Cephalexin(72-79) Cefixime(16-25)Ceftriaxone(0-12)Penicillin(30-90) Cefixime(17-27)Ceftriaxone(0-13)Cephalexin(71-80) Amoxicillin(96-100) Cefixime(87-93)Ceftriaxone(82-87) Amoxicillin(95-100) Cefixime(88-94)Cephalexin(91-95) Amoxicillin(95-100) Cefixime(88-93)Penicillin(61-64) Amoxicillin(96-100) Cephalexin(90-95) Ceftriaxone(81-86)	140
Dimethylformamid	Amoxicillin(95-100) Cephalexin(91-95) Penicillin(60-65) Amoxicillin(94-100) Penicillin(61-64)Ceftriaxone(82-88) Ampicillin(97-100) Cefixime(87-92)Ceftriaxone(80-87) Ampicillin(96-100) Cefixime(87-93)Penicillin(59-63) Ampicillin(97-100) Ceftriaxone(80-87)Penicillin(60-64) Ampicilin(96-100) Cephalexin(92-96) Penicillin(59-64) Ampicilin(95-100) Cephalexin(91-95) Ceftriaxone(82-88) Cefazoline(94-100) Cefixime(88-93)Ceftriaxone(80-85) Cefazoline(96-100) Cefixime(88-92) Penicillin(60-64) Cefazoline(95-100) Ceftrizxone(81-86)Penicillin(62-65) Cefixime(88-92)Ceftriaxone(80-87) Penicillin(63-67) Ceftriaxone(81-86)Cephalexin(91-95)Penicillin(61-64)	135
Methanol	Amoxicillin(87-94) Ceftriaxone(72-79) Ampicillin(90-92) Cefixime(80-89) Ceftriaxone(71-79) Ampicillin(90-93) Cefixime(81-90) Cephalexin(83-88) Ampicillin(91-94) Cefixime(79-88) Penicillin(82-87)	

Mobile phase	Separation(hRT - hRL)	Time (min)
	Ampicillin(92-95) Ceftriaxone(71-77)Cephalexin(85-89) Ampicillin(91-93) Cephalexin(84-88) Penicillin(81-87) Cefazoline(88-92) Ceftriaxone(72-78) Penicillin(82-86) Cefixime(81-88) Ceftriaxone(72-77)	110
Methylethylketone + acetic acid(4:1)	Amoxicillin(62-66) Ampicillin(75-81) Cefazoline(95-100) Amoxicillin(63-69) Ampicillin(76-82) Ceftriaxone(13-22)	145
Butanol- water-AcAC (20-2-1)	Amoxicillin(61-65) Ampicillin(77-82) Penicillin(71-75) Amoxicillin(63-68) Ceftriaxone(13-23) Penicillin(70-74) Amoxicillin(62-68) Ceftriaxone(13-24) Cefazoline(96-100)	72
Ethyl acetate-propanol--water (3-5-3)	Amoxicillin(63-70) Penicillin(71-75) Cefazoline(95-100) Cefixime(9-16) Cefazoline(72-83)	184
Methylethylketone + acetic acid(4:1)	Ceftriaxone(66-74) Cephalexin(82-92)	145

4. CONCLUSION

It is concluded that using the current method, the selectivity of one antibiotic from other components as well as two-component and three-component adsorption was obtained. Quantitative identification of antibiotics was also performed in multi-component mixtures after selection of appropriate isolates. The results showed that the chromatographic behaviour of antibiotics on the thin layer of zeolite clearly show that the stationary phase zeolite is valid and useful for the separation of antibiotics in thin layer chromatography.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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