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COMPATIBILITY AND STABILITY OF TERNARY ADMIXTURE OF MIDAZOLAM, DOBUTAMINE AND DOPAMINE IN 5% GLUCOSE OR 0.9% SODIUM CHLORIDE SOLUTION

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The aim of this study was to evaluate compatibility and stability of the maximum concentration used for ternary admixture containing midazolam, dobutamine and dopamine in 5% glucose and 0.9% sodium chloride solutions. The maximum concentration of each drug was 0.144 mg/ml of midazolam, 5.76 mg/ml of dobutamine and 2.88 mg/ml of dopamine in 50 ml of 5% glucose or 0.9% sodium chloride solutions. The physical compatibility of ternary admixtures was assessed using visual inspection and pH determination of ternary admixtures immediately after preparation (at 0 time) and after 24 hrs. The chemical stability was assessed using high performance thin layer chromatoghraphy (HPTLC). The method is based on HPTLC separation of the three drugs followed by densitometric measurements of their spots at 254 nm using Camag TLC Scanner 3. The mobile phase comprised ethyl acetate : n-propanol : water : glecial acetic acid (60:24:9:3, v/v/v/v). There were no visual changes (such as precipitation, gas evaluation or change in color) during 24 hrs after preparation of admixture. Also, there was no change in pH values of admixtures during that time. The results revealed chemical stability of midazolam, dobutamine and dopamine over the duration of mixing (24 hrs) in 5% glucose or 0.9% sodium chloride solutions.

INTRODUCTION

Physicochemical incompatibilities between injected drugs frequently occur in hospitals. Physicochemical incompatibilities of intravenous solutions are major concerns in medication errors[1&2]. Drug incompatibilities are frequent and may occur between active ingredients, excipients, and even tubing[3]. They emerge as color change, gas formation, turbidity and precipitation or may lead to invisible chemical reactions such as pH changes or complex reactions which can result in loss of active compounds or reduced bioavailability of the active ingredient[4]. Compatibility is not certain for drug combinations in which the compatibility is unknown or ambiguous for up to 45% of co-infusions in an intensive care units (I.C.Us.)[5]. Unfortunately there is only data describing the physical or chemical compatibility of approximately half of the possible 2-medication combinations (and virtually no data for 3 or more medication combinations) commonly used in (I.C.Us.)[6]. Intravenous drug administration in neonatal intensive care units (N.I.C.Us.) and pediatric intensive care units (P.I.C.Us.) is critical because of poor venous access, polymedication, fluid restriction and low infusion rate. Risk is further increased by inadequate information on the physicochemical compatibility of drugs[7]. Chemical compatibility requires analytical techniques such as high performance liquid chromatography to confirm at least 90% availability of both drugs in combination over the duration of mixing[8]. Midazolam, dobutamine and dopamine are commonly used in neonatal intensive care

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units. Midazolam is a short acting benzodiazepine used in NICU as sedative drug to reduce stress and avoid complications during procedures such as mechanical ventilation[9]. Midazolam is safe and effective for the treatment of uncontrollable neonatal seizures which could not be controlled by diazepam, phenytoin or phenobarbital[10]. Adverse effects of midazolam included hypotension that was successfully controlled with intropic agents (dopamine and/or dobutamine)[10]. Also, hypotension is a common medical problem in neonatal intensive care units, especially among the most premature infants[11&12]. The requires administration of dopamine and/or dobutamine as inotropic drugs. Some neonatal medical cases, need to use ternary admixture of midazolam, dobutamine and dopamine. The use of ternary admixture is advantageous as it reduce the volume of fluid that can be administered after separate administration of each drug. This is extremely important in neonates. The objective of this study was to evaluate physical compatibility and chemical stability of maximum concentrations of midazolam, dobutamine and dopamine that can be used in clinical practice in N.I.C.U. when admixed together with 5% glucose solution or 0.9% NaCl solution.

MATERIALS AND METHODS

Reagents and materials

Dormicum ampoules (Midazolam hydrochloride for injection 5 mg/ml, F.Hoffmann-La Roche Ltd., France). Dobutamine ampoules (Dobutamine hydrochloride for injection 250 mg/5 ml, EUP, for pharmaceutical and chemical industry, Egypt). Dopamine ampoules (Dopamine hydrochloride for injection 200 mg/5 ml, EUP, for pharmaceutical and chemical industry, Egypt). 5% glucose intravenous solution and 0.9% sodium chloride intravenous solution. Thin layer chromatoghraphy aluminium sheets (precoated with silica gel 60 F_{254} plates 20x20 with 0.250 mm layer thickness, E. Merck, Germany). Ethyl acetate, n-propanol and acetic acid glacial (All chemicals used were of pharmaceutical grade).

Instruments

Digital pH meter (Jenway Ltd., Feslted, Dunmow, U.K.) and Camag TLC-Scanner III (Switzerland, comprising of Camag Linomat 5 applicator, Camag TLC Scanner 3, Camag WinCATS software, Hamilton syringe (100 µl), Camag Reprostar 3, Camag UV Cabinet).

Preparation of admixtures

Midazolam admixture was prepared by transferring 1.44 ml solution from dormicum ampoules to volumetric flask 50 ml. The volume was completed to 50 ml with 5% glucose or 0.9% sodium chloride solution. The final concentration of midazolam was 0.144 mg/ml.

Dobutamine admixture was prepared by transferring 5.76 ml solution from dobutamine ampoules to volumetric flask 50 ml. The volume was completed to 50 ml with 5% glucose or 0.9% sodium chloride solution. The final concentration of dobutamine was 5.76 mg/ml.

Dopamine admixture was prepared by transferring 3.6 ml solution from dopamine ampoule to volumetric flask 50 ml. The volume was completed to 50 ml with 5% glucose or 0.9% sodium chloride solution. The final concentration of dopamine was 2.88 mg/ml.

Ternary admixture of midazolam, dobutamine and dopamine was prepared by transferring 1.44 ml of midazolam ampoules (equivalent to 7.2 mg) to 50 ml volumetric flask. The flask was shaken gently after adding small amount of 5% glucose or 0.9% sodium chloride solution. To the same flask, 5.76 ml of dobutamine ampoule (equivalent to 288 mg) was added and mixed carefully by gentle shaking. At the end, 3.6 ml of dopamine ampoule (equivalent to 144 mg) was added and mixed carefully. The volume was adjusted with infusion fluids. The final concentration of midazolam was 0.144 mg/ml, dobutamine was 5.76 mg/ml and dopamine was 2.88 mg/ml.

The temperature of preparation and storage were at room temperature.

Investigation of physical compatibility of admixtures

The physical compatibility of admixture was assessed using visual inspection and pH determination of admixture immediately after preparation (at 0 time) and after 24 hrs. Visual inspection was conducted to detect precipitation (against a black background), gas formation, turbidity or color change (against a

white background and compare with color of water) immediately after preparation of admixtures and then after 24 hrs.

Investigation of chemical stability of admixtures using Camag TLC-Scanner III

A large number of publications have appeared in the last decade on the use of HPTLC (high performance thin layer chromatography) for stability studies[13-17]. Chemical stability of admixture was assessed by comparing between R_f, peak area and absorbance of each drug immediately after preparation of ternary admixture and after 12 and 24 hrs in 5% glucose or 0.9% sodium chloride solution.

Chromatographic conditions

Three microlitres of solutions of drugs was applied to plates (20x10 cm) by means of a Linomat V automatic spotter, equipped with a 100 µL syringe and operated with settings of band length, 4 mm; distance between bands, 10 mm; distance from the plate edge, 10 mm; and distance from the bottom of the plate, 10 mm at room temperature (25±2°C). The plate was developed in a twin trough chamber previously saturated for 60 min with mobile phase to ensure good reproducibility for peak shapes and areas of drugs by using ethyl acetate : n-propanol : water : glacial acetic acid, 60:24:9:3, (v/v/v/v) as mobile phase to 8.0 cm. The developed TLC plates were dried in a current of air. The slit dimension was kept at 3.0 mm x 0.45 mm and the scanning speed was 10 mm/s. Densitometric scanning was performed using a Camag TLC scanner III in the absorbance mode at 254 nm and operated by CATS software.

RESULTS AND DISCUSSION

Physical compatibility of ternary admixture

There was no precipitation, gas evaluation, change in colour or change in pH of ternary admixture at zero time and after 24 hrs in 5% glucose solution or 0.9% sodium chloride solution. The pH values are presented in table 1.

Chemical stability of admixtures by Camag TLC-Scanner III

5% glucose solution

The mobile phase consisting of ethyl acetate : *n*-propanol : water : glecial acetic acid 60:24:9:3 (*v*/*v*/v/v) gave good resolution for midazolam, dobutamine and dopamine.

By densitometric evaluation "Chromatogram evaluation": There was no indication of degradation and no unknown peaks were observed on TLC chromatogram at 0, 12 and after 24 hrs.

Table 2 presents R_f values and peak areas of midazolam alone and in ternary admixture of 5% glucose solution during 24 hrs. It appears that the R_f values of midazolam at 0.64±0.01 didn't change during 24 hrs. Peak areas of midazolam in ternary admixture of 5% glucose solution was within the range during 24 hrs. This will agree with previously reported results[18&19] that midazolam is stable in 5% glucose solution for 24 hrs.

Table 3 presents R_f values and peak areas of dobutamine alone and in ternary admixture of 5% glucose solution during 24 hrs. It appears that the R_f values of dobutamine at 0.76±0.01 didn't change during 24 hrs. Peak areas of dobutamine in ternary admixture of 5% glucose solution was within the range during 24 hrs. This is in consistent with the reported results[20&21] that dobutamine is stable in 5% glucose solution for 24 hrs.

Table 4 presents R_f values and peak areas of dopamine alone and in ternary admixture of 5% glucose solution during 24 hrs. It appears that the R_f values of dopamine at 0.18±0.01 didn't change during 24 hrs. Peak areas of dopamine in ternary admixture of 5% glucose solution was within the range during 24 hrs. This is in agreement with fore mentioned results[21-23] that dopamine is stable in 5% glucose solution for 24 hrs.

Figure 1 show TLC chromatograms of maximum concentrations of midazolam alone in 5% glucose solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peaks were observed.

Figure 2 show TLC chromatograms of maximum concentrations of dobutamine alone in 5% glucose solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peaks were observed.

Table 1: pH values of maximum concentration of midazolam, dobutamine and dopamine in 5% glucose and 0.9% sodium chloride solutions.

Admixtures of maximum concentration of drugs	Color		pH (Mean ± S.D.)		Precipitation, turbidity or gas formation	
	At 0 hr	After 24 hr	At 0 hr	After 24 hr	At 0 hr	After 24 hr
1- Midazolam in 5% glucose solution	Colorless	Colorless	4.63 ± 0.03	4.60 ± 0.03	No	No
2- Dobutamine in 5% glucose solution	Colorless	Colorless	4.67 ± 0.01	4.64 ± 0.01	No	No
3- Dopamine in 5% glucose solution	Colorless	Colorless	4.87 ± 0.01	4.83 ± 0.01	No	No
4- Ternary admixture of Midazolam, dobutamine and dopamine in 5% glucose solution	Colorless	Colorless	4.65 ± 0.01	4.62 ± 0.02	No	No
5- Midazolam in 0.9% sodium chloride solution	Colorless	Colorless	4.83 ± 0.03	4.80 ± 0.01	No	No
6- Dobutamine in 0.9% sodium chloride solution	Colorless	Colorless	5.06 ± 0.02	5.05 ± 0.01	No	No
7- Dopamine in 0.9% sodium chloride solution	Colorless	Colorless	5.17 ± 0.03	5.15 ± 0.02	No	No
8- Ternary admixture of midazolam, dobutamine and dopamine in 0.9% sodium chloride solution	Colorless	Colorless	4.78 ± 0.01	4.75 ± 0.03	No	No

Mean: Mean of three experiments. S.D.: Standard deviation.

Table 2: R_f values and peak areas of midazolam alone and ternary admixture of 5% glucose solution.

Admixtures of 5% glucose solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Midazolam alone in 5% glucose solution.	0.64	0.64	0.64	4909 ± 104 (%RSD= 2.1)	4926 ± 122 (%RSD= 2.5)	4886 ± 131 (%RSD= 2.7)
Midazolam with dobutamine and dopamine in ternary admixture of 5% glucose solution	0.64	0.64	0.64	4950 ± 130 (%RSD= 2.6)	4959 ± 117 (%RSD= 2.3)	4945 ± 140 (%RSD= 2.8)

Table 3: R_f values and peak areas of dobutamine alone and in ternary admixture of 5% glucose solution.

Admixtures of 5% glucose solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Dobutamine alone in 5% glucose solution.	0.76	0.76	0.76	10996 ± 251 (%RSD= 2.3)	10616 ± 230 (%RSD= 2.2)	10732 ± 221 (%RSD= 2.1)
Dobutamine with midazolam and dopamine in ternary admixture of 5% glucose solution	0.76	0.76	0.76	10935 ± 238 (%RSD= 2.2)	11124 ± 219 (%RSD= 2)	11015 ± 221 (%RSD= 2)

Table 4: R_f values and peak areas of dopamine alone and in ternary admixture of 5% glucose solution.

Admixtures of 5% glucose solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Dopamine alone in 5% glucose solution.	0.18	0.18	0.18	9881 ± 230 (%RSD= 2.3)	9656 ± 211 (%RSD= 2.2)	9791 ± 222 (%RSD= 2.3)
Dopamine with midazolam and dobutamine in ternary admixture of 5% glucose solution	0.18	0.18	0.18	9907 ± 240 (%RSD= 2.4)	10107 ± 220 (%RSD= 2.2)	10059 ± 219 (%RSD= 2.2)

R_f : Retention factor, R_f = Distance of center of spot from starting point / Distance of solvent front from starting point.
Mean: Mean of five experiments
S.D.: Standard Deviation
%RSD (Relative Standard Deviation) = [S.D. Standard Deviation / mean] x100
At 0 hr: immediately after preparation of admixture
Unit of peak area: absorbance unit (AU).

Figure 3 show TLC chromatograms of maximum concentrations of dopamine alone in 5% glucose solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peaks were observed.

Figure 4 show TLC chromatograms of maximum concentrations of midazolam, dobutamine and dopamine in ternary admixture of 5% glucose solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peaks were observed.

Figures 5-7 display absorption spectra of maximum concentrations of midazolam, dobutamine and dopamine in ternary admixture of 5% glucose solution at 0, 12 and 24 hrs. It appears that the absorption spectra of midazolam, dobutamine and dopamine didn't change during 24 hrs with the same wavelength at λ_{max}= 231 nm, 280 nm and 281 nm, respectively. No change in the spectra was detected over the study period.

0.9% sodium chloride solution

The mobile phase consisting of ethyl acetate : *n*-propanol : water : glecial acetic acid 60:24:9:3 (*v*/*v*/v/v) gave good resolution for midazolam, dobutamine and dopamine.

By densitometric evaluation "Chromatogram evaluation": There was no indication of degradation and no unknown peaks were observed on TLC chromatogram at 0, 12 and after 24 hrs.

Table 5 presents R_f values and peak areas of maximum concentration of midazolam alone and in ternary admixture of 0.9% sodium chloride solution during 24 hrs. It appears that the R_f values of midazolam at 0.64±0.01 didn't change during 24 hrs. Peak areas of midazolam in ternary admixture of 0.9% sodium chloride solution were within the range during 24 hrs. This is consistent with the previously reported result[19] revealing that midazolam is stable in 0.9% sodium chloride solution for 24 hrs.

Table 6 presents R_f values and peak areas of maximum concentration of dobutamine alone and in ternary admixture of 0.9% sodium chloride solution during 24 hrs. It appears that the R_f values of dobutamine at 0.81±0.01 didn't change during 24 hrs. Peak areas of dobutamine in ternary admixture of 0.9% sodium chloride solution were within the range during 24 hrs. This is consistent with the previously reported results[20&21] that dobutamine is stable in 0.9% sodium chloride solution for 24 hrs.

Table 7 presents R_f values and peak areas of maximum concentration of dopamine alone and in ternary admixture of 0.9% sodium chloride solution during 24 hrs. It appears that the R_f values of dopamine at 0.43±0.01 didn't change during 24 hrs. Peak areas of dopamine in ternary admixture of 0.9% sodium chloride solution were within the range during 24 hrs. The results are in agreement with previously results[21&23] that dopamine is stable in 0.9% sodium chloride solution for 24 hrs.

Figure 8 show densitograms of maximum concentrations of midazolam alone in 0.9% sodium chloride solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peak can be observed.

Figure 9 show densitograms of maximum concentrations of dobutamine in 0.9% sodium chloride solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peak can be observed.

Figure 10 show densitograms of maximum concentrations of dopamine in 0.9% sodium chloride solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peak can be observed.

Figure 11 show densitograms of maximum concentrations of midazolam, dobutamine and dopamine in ternary admixture of 0.9% sodium chloride solution at 0, 12 and after 24 hrs. There was no indication of degradation and no unknown peak can be observed.

Figures 12-14 display absorption spectra of maximum concentrations of midazolam, dobutamine and dopamine in ternary admixture of 0.9% sodium chloride solution at 0, 12 and 24 hrs. It appears that the absorption spectra of midazolam, dobutamine and dopamine didn't change during 24 hrs with the same wavelengths at 231 nm, 280 nm and 281 nm respectively. No significant change in the spectra can be detected during the study period.

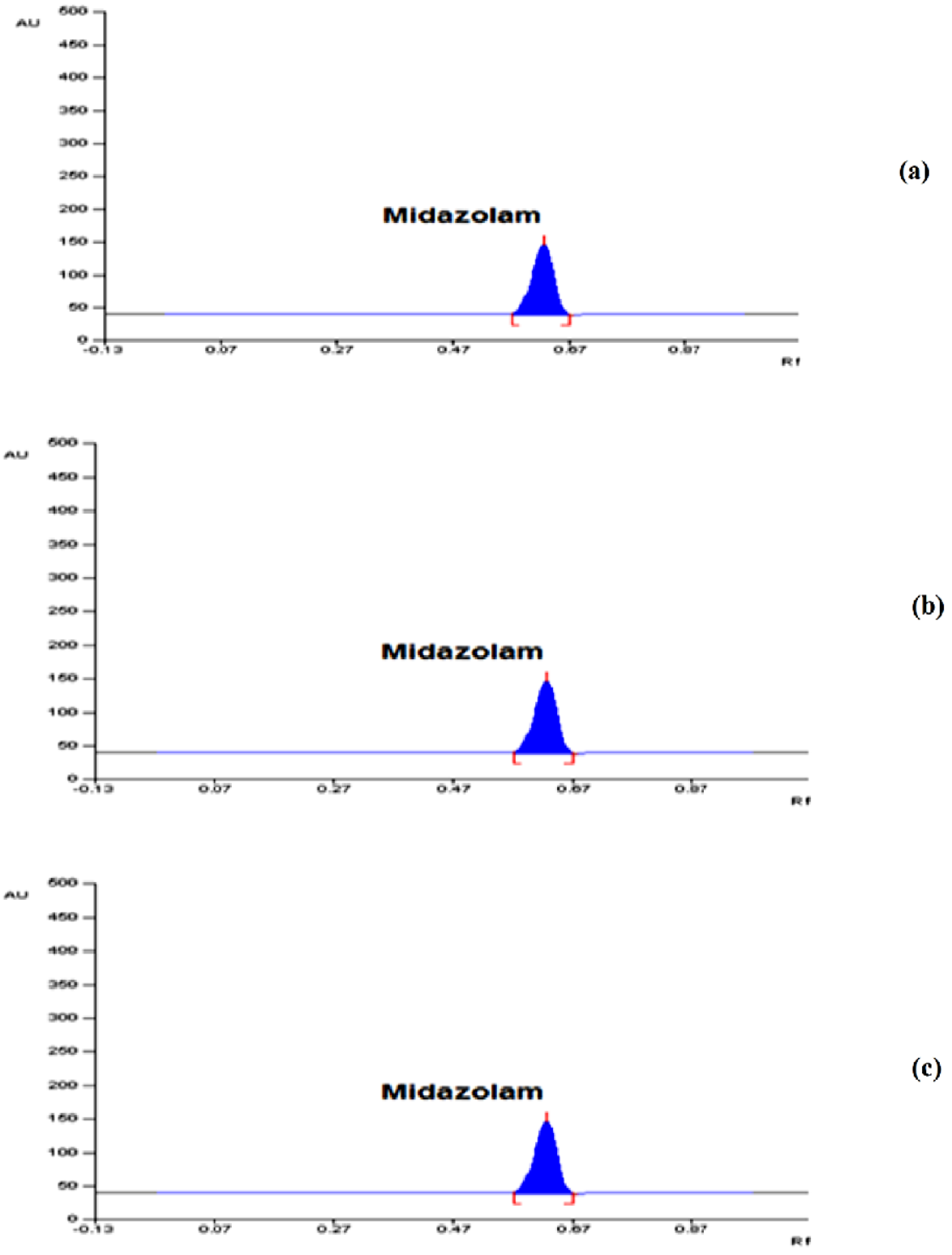

Fig. 1: TLC chromatograms of maximum concentration of midazolam in 5% glucose solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

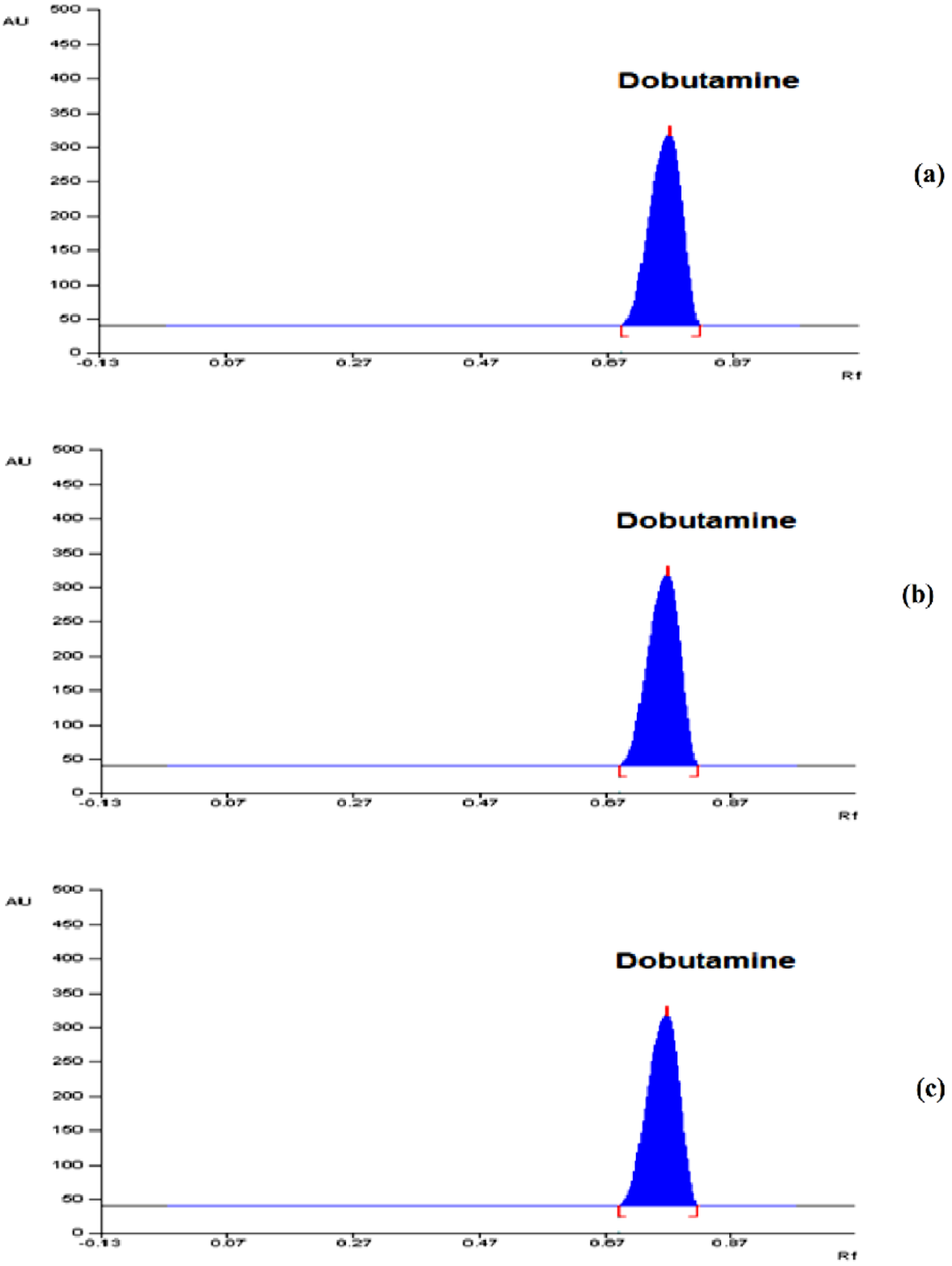

Fig. 2: TLC chromatograms of maximum concentration of dobutamine in 5% glucose solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

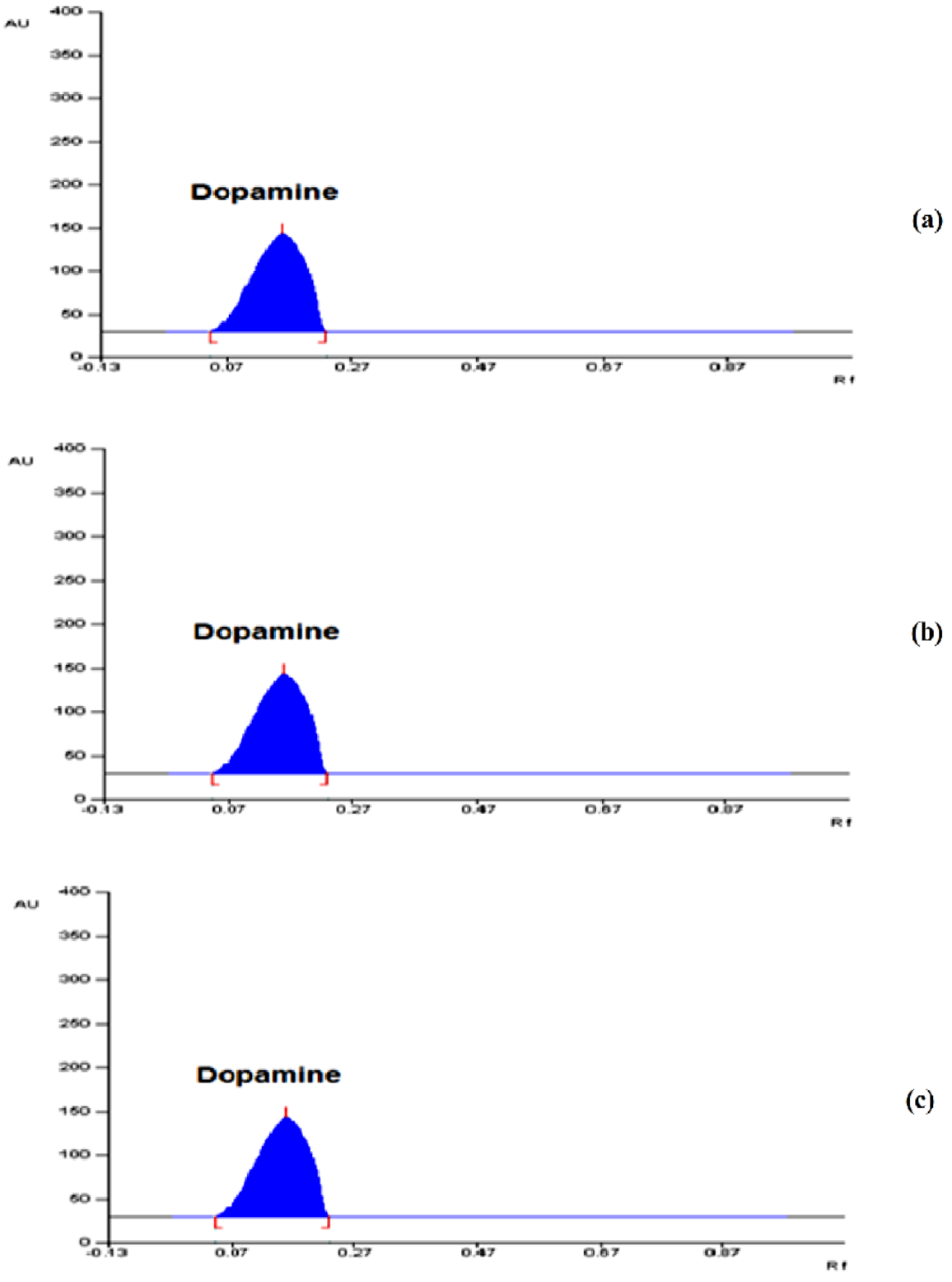

Fig. 3: TLC chromatograms of maximum concentration of dopamine in 5% glucose solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

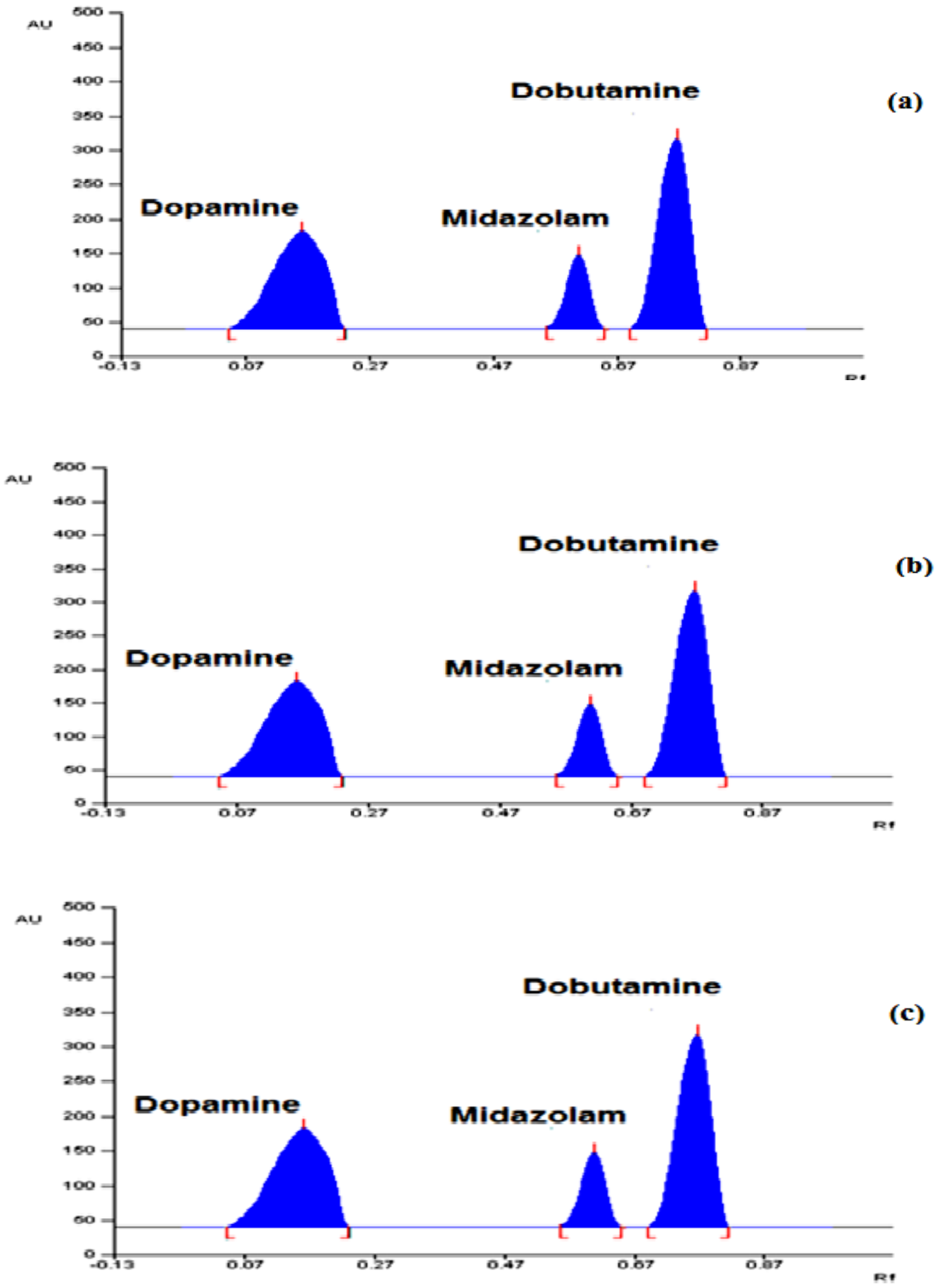

Fig. 4: TLC chromatogram of maximum concentration of midazolam, dobutamine and dopamine in ternary admixture of 5% glucose solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

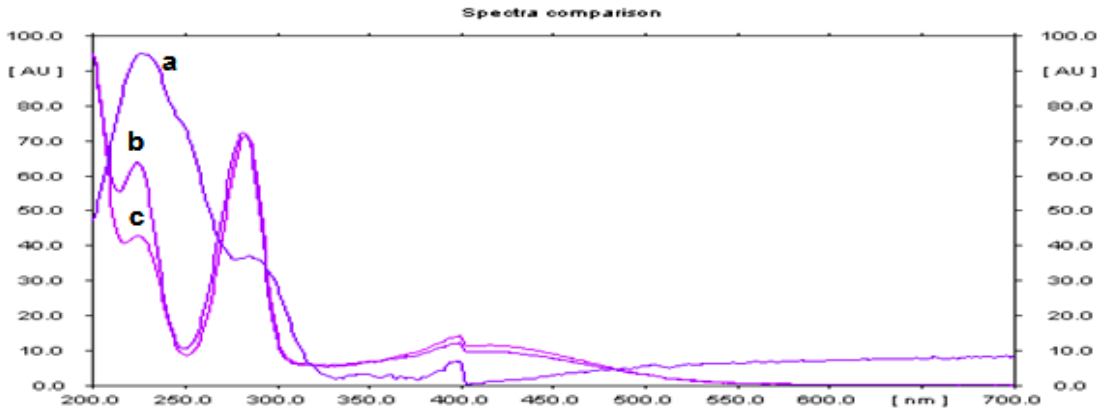

Fig. 5: Absorption spectra of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 5% glucose solution at 0 hr.

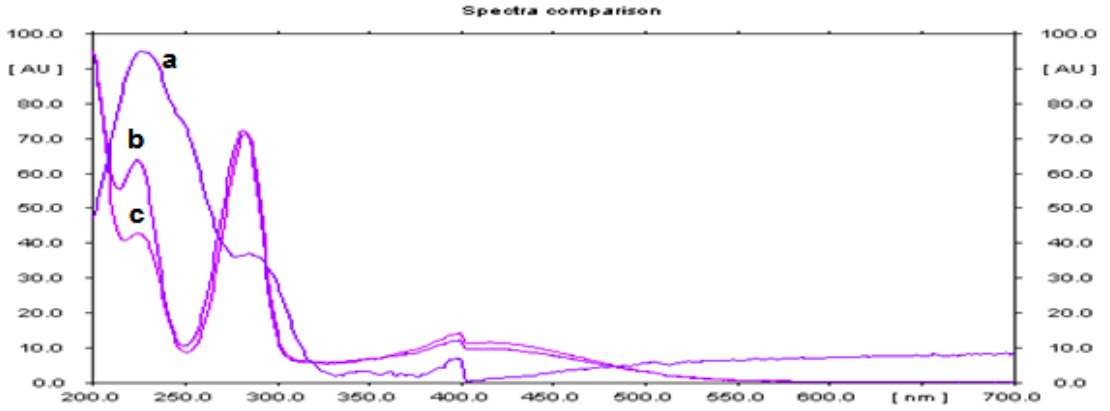

Fig. 6: Absorption spectra of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 5% glucose solution after 12 hr.

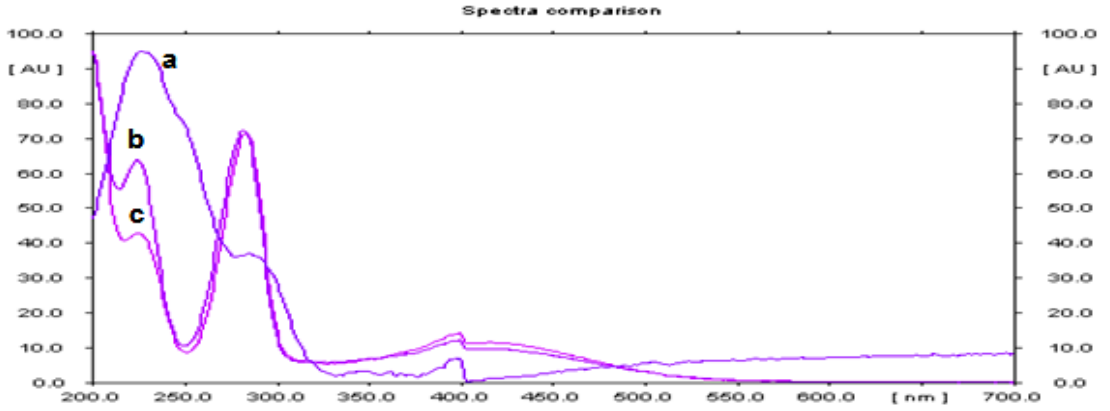

Fig. 7: Absorption spectra of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 5% glucose solution after 24 hr.

Table 5: R_f values and peak areas of midazolam alone and in ternary admixture of 0.9% sodium chloride solution.

Admixtures of 0.9% sodium chloride solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Midazolam alone in 0.9% sodium chloride solution.	0.64	0.64	0.64	4730 ± 99 (%RSD= 2.1)	4688 ± 110 (%RSD= 2.3)	4659 ± 95 (%RSD= 2)
Midazolam with dobutamine and dopamine in ternary admixture of 0.9% sodium chloride solution.	0.64	0.64	0.64	4729 ± 96 (%RSD= 2)	4779 ± 90 (%RSD= 2)	4743 ± 102 (%RSD= 2.2)

Table 6: R_f values and peak areas of dobutamine alone and in ternary admixture of 0.9% sodium chloride solution.

Admixtures of 0.9% sodium chloride solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Dobutamine alone in 0.9% sodium chloride solution.	0.81	0.81	0.81	10809 ± 225 (%RSD= 2.1)	10695 ± 230 (%RSD= 2.2)	10993 ± 219 (%RSD= 2)
Dobutamine with midazolam and dopamine in ternary admixture of 0.9% sodium chloride solution.	0.81	0.81	0.81	10911 ± 245 (%RSD= 2.3)	11140 ± 240 (%RSD= 2.2)	10818 ± 237 (%RSD= 2.2)

Table 7: R_f values and peak areas of dopamine alone and in ternary admixture of 0.9% sodium chloride solution.

Admixtures of 0.9% sodium chloride solution	R_f (mean ± S.D.) (S.D. = 0.01)			Peak area (mean ± S.D.)		
	0 hr	12 hr	24 hr	0 hr	12 hr	24 hr
Dopamine alone in 0.9% sodium chloride solution.	0.43	0.43	0.43	9746 ± 217 (%RSD= 2.2)	9955 ± 234 (%RSD= 2.4)	9846 ± 236 (%RSD= 2.4)
Dopamine with midazolam and dobutamine in ternary admixture of 0.9% sodium chloride solution.	0.43	0.43	0.43	9897 ± 234 (%RSD= 2.4)	9917 ± 239 (%RSD= 2.4)	9818 ± 230 (%RSD= 2.3)

R_f : Retention factor, R_f = Distance of center of spot from starting point/ Distance of solvent front from starting point.
Mean: Mean of five experiments
S.D.: Standard Deviation
%RSD (Relative Standard Deviation) = [S.D. Standard Deviation / mean] x100
At 0 hr: immediately after preparation of admixture
Unit of peak area: absorbance unit (AU)

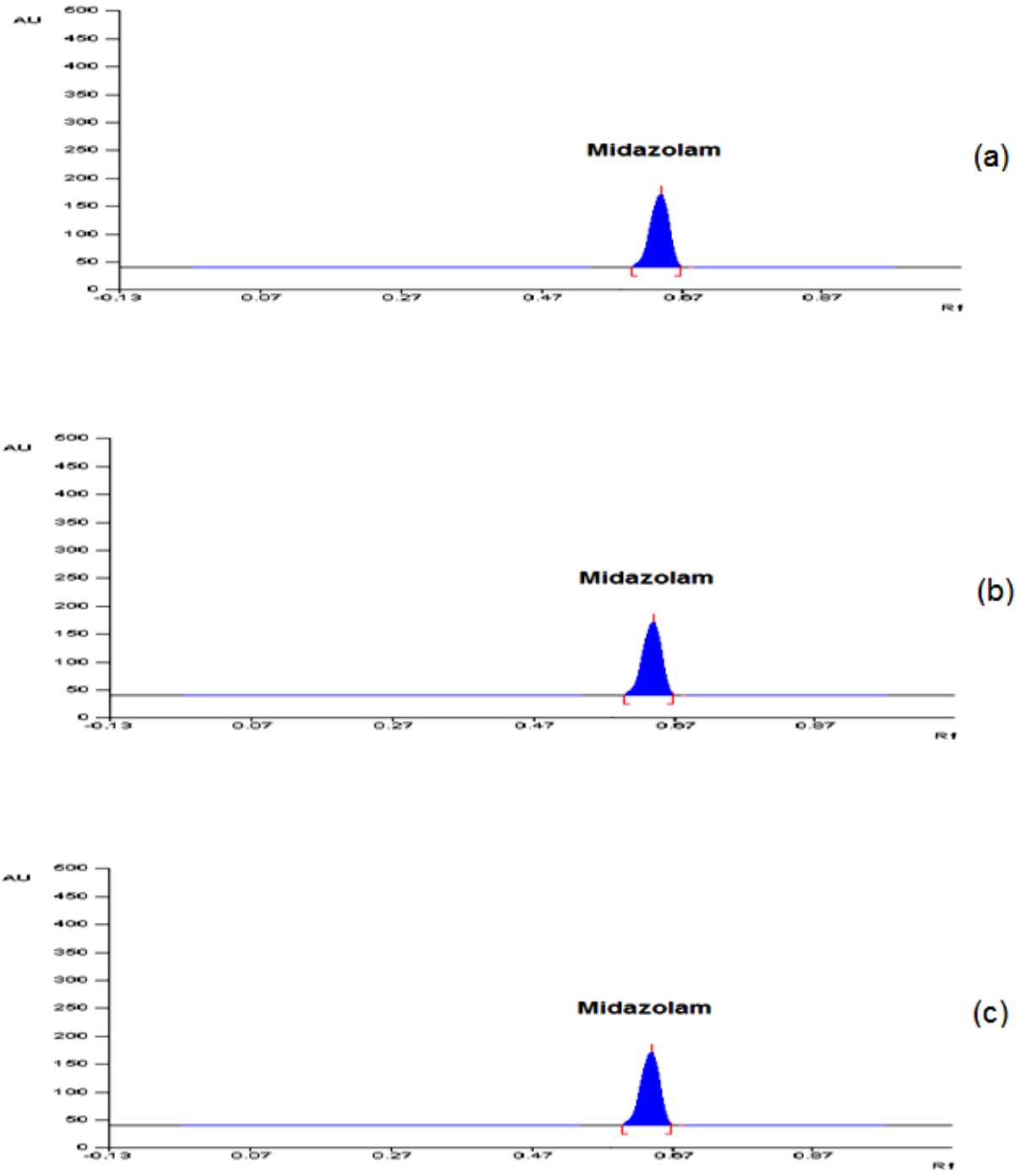

Fig. 8: TLC chromatograms of the maximum concentration of midazolam in 0.9% sodium chloride solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

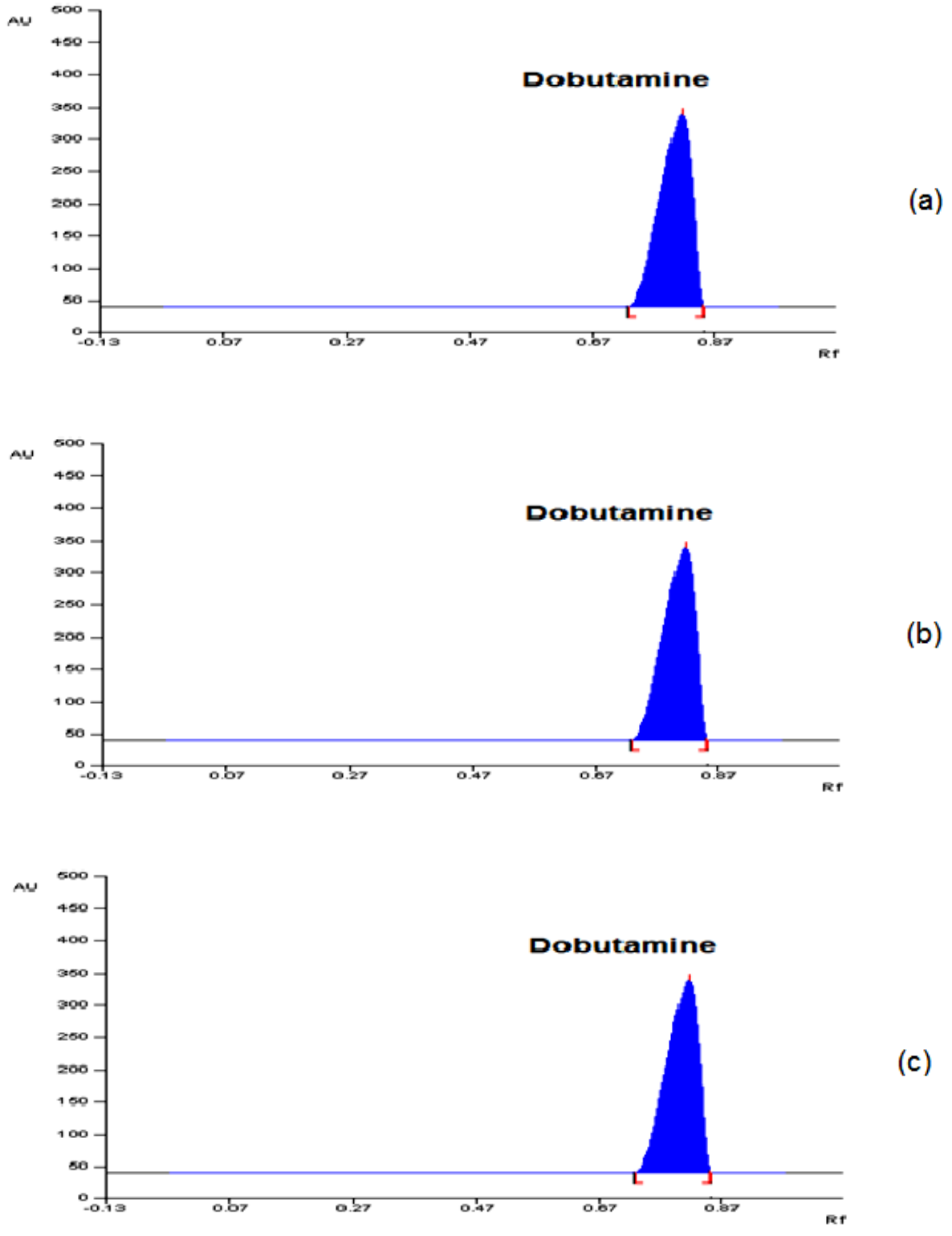

Fig. 9: TLC chromatograms of the maximum concentration of dobutamine in 0.9% sodium chloride solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

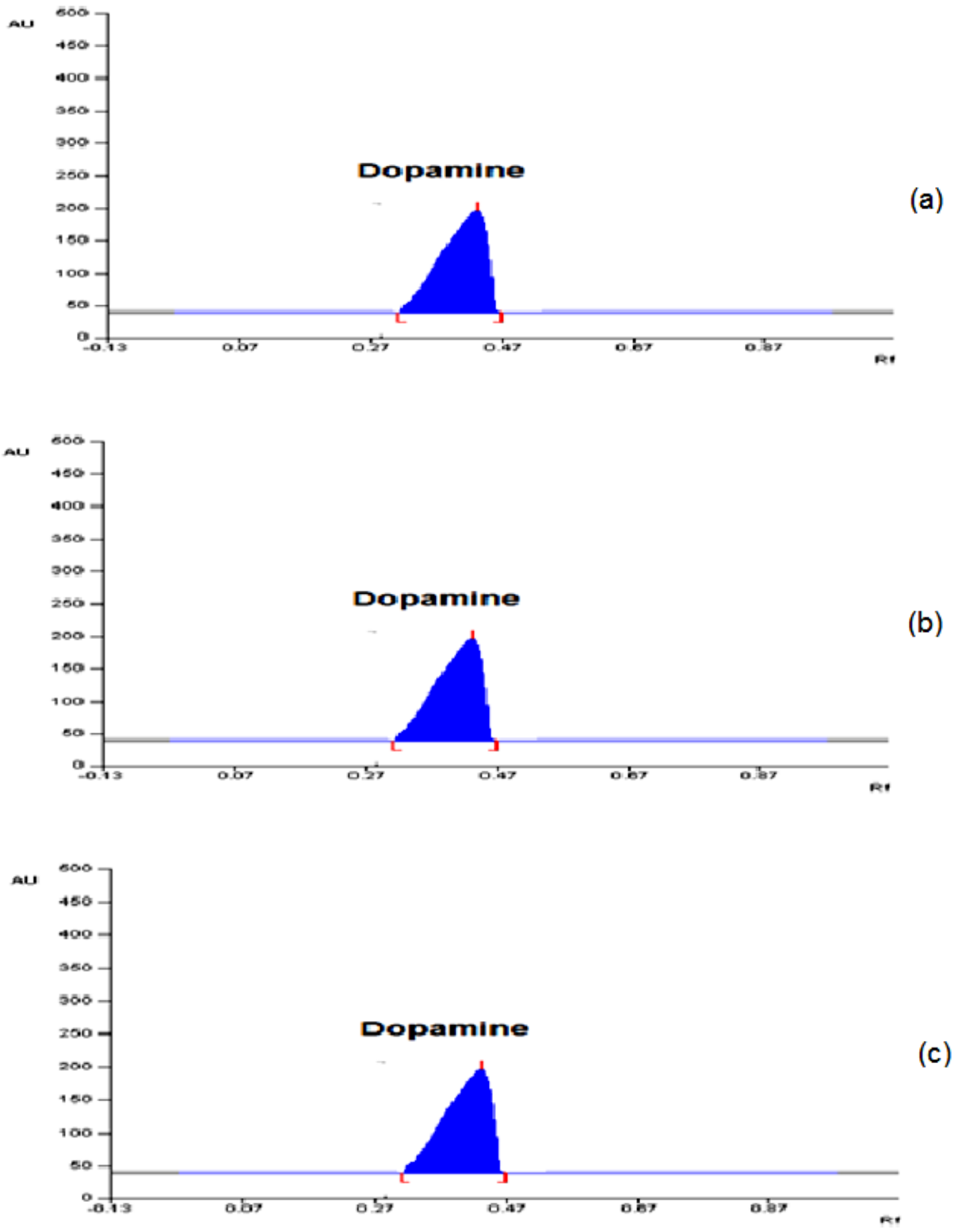

Fig. 10: TLC chomatograms of the maximum concentration of dopamine in 0.9% sodium chloride solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

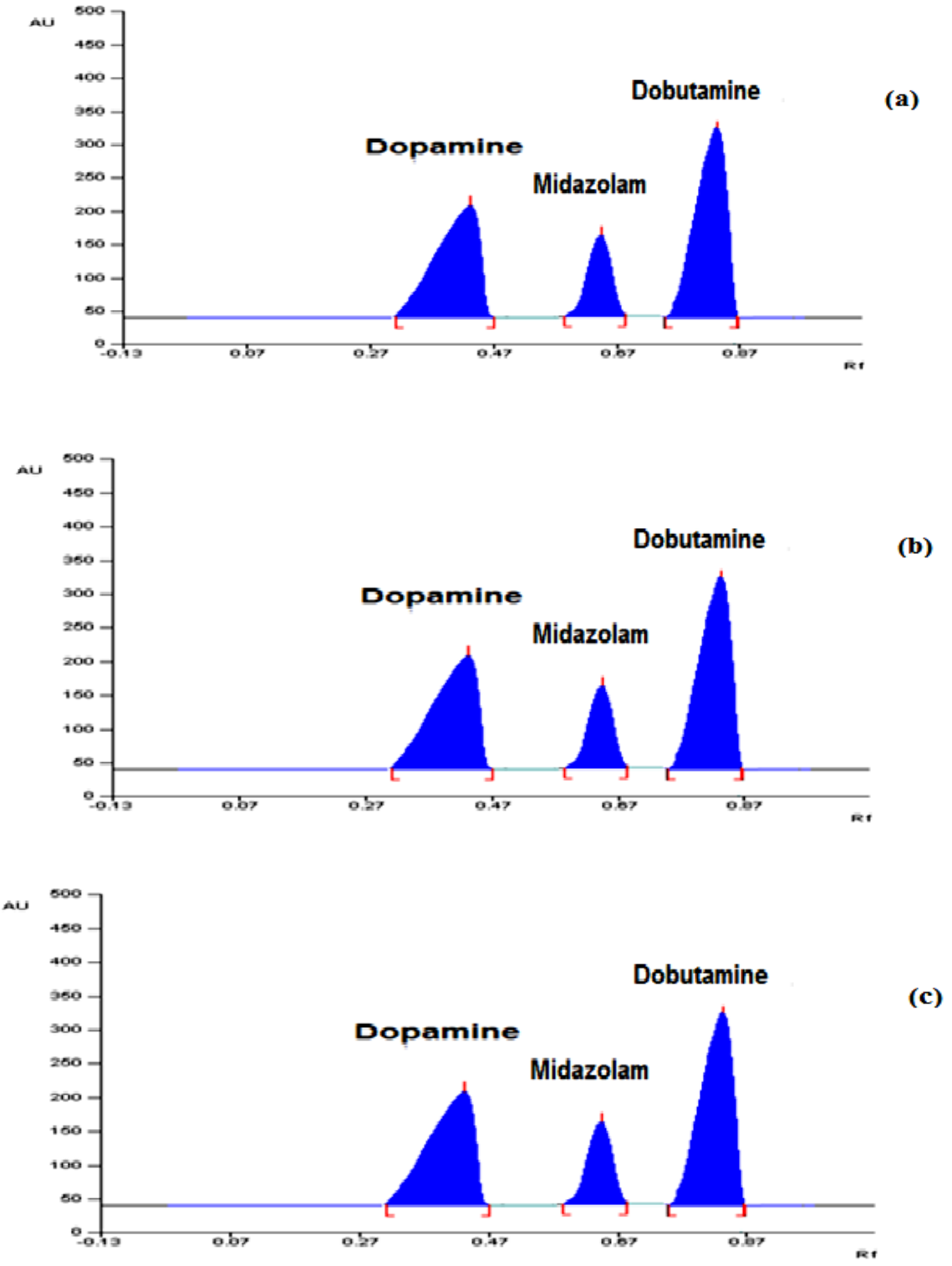

Fig. 11: TLC chromatogram of maximum concentration of midazolam, dobutamine and dopamine in ternary admixture of 0.9% sodium chloride solution: a) at 0 hr. b) after 12 hr. c) after 24 hr.

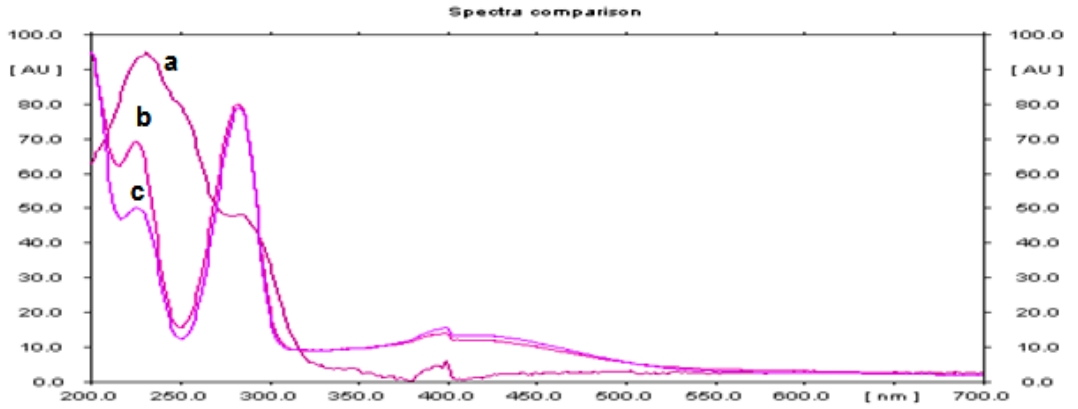

Fig. 12: Absorption spectra of maximum concentration of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 0.9% sodium chloride solution at 0 hr.

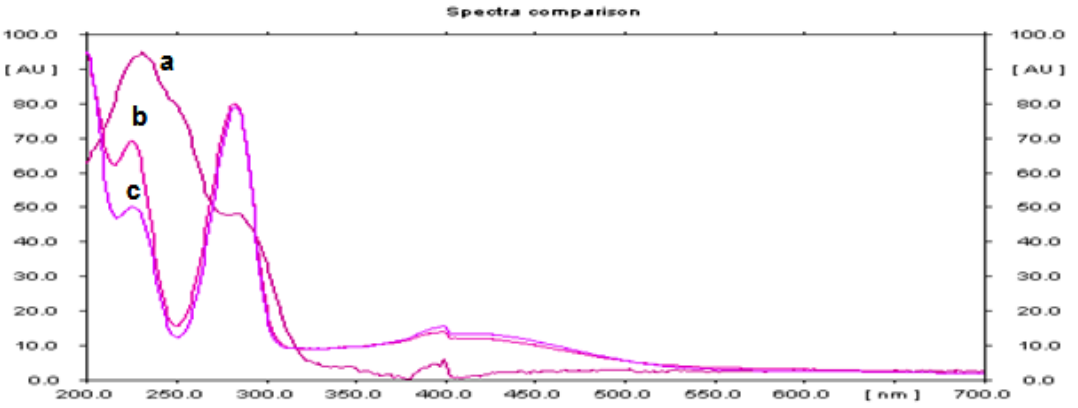

Fig. 13: Absorption spectra of maximum concentration of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 0.9% sodium chloride solution after 12 hr.

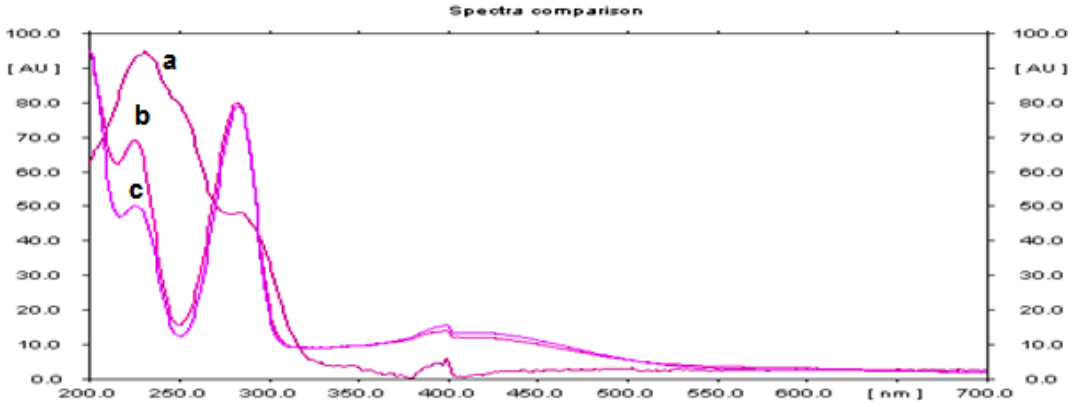

Fig. 14: Absorption spectra of maximum concentration of midazolam (a), dobutamine (b) and dopamine (c) in ternary admixture of 0.9% sodium chloride solution after 24 hr.

Conclusions

In this study, precise and accurate HPTLC method suitable for stability evaluation of midazolam HCL combined with dobutamine HCL and dopamine HCL is described. The physical appearance of the solutions remained constant during the study period, without any visible discoloration, cloudiness, or precipitation. There was no change in pH value during 24 hrs. There was no indication of degradation and no unknown peaks can be observed on TLC chromatogram at 0, 12 and after 24 hrs. The absorption spectra of midazolam, dobutamine and dopamine didn't change during 24 hrs with the same λ_{max} at 231 nm, 280 nm and 281 nm respectively. The results indicated the compatibility between midazolam, dobutamine and dopamine in ternary admixture of 0.9% sodium chloride solution for 24 hrs.

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نشرة العلوم الصيدلية
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توافق وثبات المخلوط الثلاثي لعقار الميدازولام والدوبيوتامين والدوبامين في محلول جلوكوز 5% أو محلول كلوريد الصوديوم ٠,٩%

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الهدف من هذه الدراسة هو تقييم مدى توافق وثبات التركيزات العالية التى يمكن استخدامها لعمل المخلوط الثلاثى من مادة الميدازولام والدوبيوتامين والدوبامين فى محلول الجلكوز 5% أو فى محلول كلوريد الصوديوم ٠,٩%. التركيزات العالية المستخدمة من مادة الميدازولام هي ٠,١٤٤ ملليجرام/ ملليلتر ومن مادة الدوبيوتامين هى ٥,٧٦ ملليجرام/ ملليلتر ومن مادة الدوبامين هى ٢,٨٨ ملليجرام/ ملليلترفى ٥٠ ملليلتر من محلول الجلكوز 5% أو محلول كلوريد الصوديوم ٠,٩%. التوافق الفيزيائى للمخلوط الثلاثى يتم تقييمة عن طريق الفحص البصري وكذلك تم تعين الأس الهيدروجينى للمخلوط الثلاثى فور تحضيره وبعد مرور٢٤ ساعة. الثبات الكيميائى تم تقييمة عن طريق استخدام كروماتوجرافيا الطبقة الرقيقة. وتعتمد الطريقة على فصل الثلاث أدوية ثم قياس شدة الكثافة الضوئية لكل نقطة منهم عند ٢٥٤ نانوميتر فور تحضيره هذا المخلوط الثلاثى وبعد مرور ١٢ و٢٤ ساعة بأستخدام جهازكروماتوجرافيا الطبقة الرقيقة (كماج٣). عن طريق استخدام الوسط المتحرك من الاثيل اسيتات : ن بروبانول : الماء : حمض الخليك بنسبة ٦٠:٢٤:٩:٣ على التوالى. وقد لوحظ أن الفحص البصرى للمخلوط الثلاثى خلال ٢٤ ساعة التالية للتحضيرلم يحدث أي راسب أو تصاعد غاز أو تغير فى اللون. وكذلك لم يحدث تغير لقيمة الأس الهيدروجينى للمخلوط الثلاثي. وبذلك تبين وجود ثبات كيميائى لكل من الميدازولام والدوبيوتامين والدوبامين اثناء هذة المدة فى محلول الجلكوز5% او محلول كلوريد الصوديوم ٠,٩%.