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Research Article

EVALUATION OF DISSOLUTION STUDY OF WEAKLY ACIDIC DRUG PABA IN BINARY SOLVENT MIXTURE BY SPECTROPHOTOMETRIC METHOD

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ABSTRACT

Para Amino Benzoic Acid (PABA) is a weakly acidic drug. So, Spectrophotometric method is applicable for determination of dissociation constant for PABA. Spectrophotometrically dissociation constant (pKa) of the indicator acid, PABA in 5,10,20,30 and 40 wt. % 1-butanol – water mixtures at 24.5±0.5ºC were measured. The pure indicator acid and potassium salt of indicator acid show maxima at 360 nm and 400nm. The spectrophotometic data have been analyzed in term of an ion – pair intermediate model. The experimental values of ЄIn- potassium salt of indicator acid and the derived values of intercept of ЄIn- values using equation,
shows a good consistency ,suggesting the ion-pair intermediate model is applicable in the present instance. The maximum drop in pka was found to occur around 20 wt. % 1-butanol- water mixtures. This has been explained as due to increase in solvation energy for anion of the acid by London-dispersion force mechanism. The drastic increase in pka values above 20 wt% 1-butanol has been assumed to be due to decrease in dielectric constant of the medium. The values of pKa and pH are especially important to understand solubility profile, absorption, distribution of drug and drug product. Obviously it can mention here that this research work will helpful so greatly in the field of dissolution study, pre-formulation study, formulation & different types of dosage form development and drug delivery of drugs are weakly acidic in nature.

INTRODUCTION

The study of aqueous mixtures has drawn an early attention of many investigators for various physiochemical properties of electrolyte solutions. Such studies in aqueous mixtures are standard potentials of the electrodes, solubility of single ions and electrometric method of determination of dissociation constant of weak acids. It has been observed by some workers i.e Glover [(1)], Fong and Grunwald.[(2)] that the dissociation constants of charged and uncharged weak acids of different types pass through a maximum when the solvent composition of acetone-water, ethanol-water, methanol-water system is varied. The appearance of the maximum can therefore be attributed to the unusual influence of water on acid-base processes taking place in the solvent mixtures containing water as one of the component. According to the view of Frank and Wen.[(3)] the remarkable properties of liquid water are to be attributed to the existence of self-stabilizing three-dimensional hydrogen-bonded flickering clusters with lifetime of the order of 10^{-11} seconds. These entities are maximally hydrogen-bonded and voluminous, making water an open-structured liquid full of cavities. In equilibrium with the structured solvent is another form of water, not hydrogen-bonded and relatively dense. Franks and lves.[(4)] reviewed in detail the structure of alcohol-water mixtures. From the simple view, the hydrophobic hydrocarbon chain in alcohol may be regarded as opposing the effect of the hydrophilic-OH group in its attempt to pull the molecule into solution[(5)]. The hydroxyl group can form hydrogen bonds with the solvent molecules, acting either as donor or as acceptor. They have shown that the excess thermodynamic factors are consistent with the view that this is just the region in which the order disorder relationships in the structure of mixed solvent are undergoing the most striking changes[(6)]. These structural alteration seem to be particularly pronounced in t-butanol-water mixtures J. Ghasemi[(7)].

MATERIALS AND METHODS

Solvents and Reagents

Para-Amino Benzoic Acid (MERCK, 98% pure), KOH (E. MERCK, DARMSTADT), HNO_3 (E. MERCK, DARMSTADT. 65% pure), Butanol-1 (MERCK, DARMSTADT, 99% pure) and demineralized water.

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Purification of Solvents and Sample

Demineralized water, distilled twice from a Pyrex glass still, was used. The specific conductivity of the water varied between 1.5 X 10^{-6} and 2.5 X 10^{-6} mhos/cm.

Preparation of recrystallized Para Amino Benjoic Acid

Para Amino Benjoic Acid was purified by recrystalization from butanol. The vacuum dried product melted at 113.5ºC (Literature value 114ºC). The recrystallized Para Amino Benzoic Acid was kept over $CaCl_2$ in a vacuum desiccators. Analysis of the recrystallized sample gave a purity of 100.0 % . The recrystallized sample was carried out free from moisture and carbon dioxide.

Preparation of solution of Para Amino Benzoic Acid and K-salt of PABA

The initial concentration Para Amino Benzoic Acid on of was known by weight and the solvent was 1-butanol – water mixtures. The experimental solutions were made by dilution of concentrated solution with the help of micropipette. A solution of KOH was prepared by weight and the solvent was 1-butanol– water mixtures. The actual strength of KOH was known by titration with succinic acid by using phenolphthalein indicator. Dilute solution was made by dilution of concentrated KOH solution. The initial concentration of K-salt of Para Amino Benjoic Acid was known by weight and the solvent was the solution of KOH. The experimental solutions were made by dilution of concentrated solution and the solvent used was dilute solution of KOH. All other chemicals were high purity reagent grade products.

Spectrophotometric Measurements

The spectra and all absorbance values reported in the thesis were obtained using two spectrophotometers (one is SHIMADZU UV-Visible Recording Spectrophotometer and another Spectro UV-VIS RS spectrophotometer) by selecting wavelength length range 250-600nm. Teflon capped silica cells of 1.00 cm. light path were used throughout. The cells were calibrated and the constancy of calibration was checked periodically by measuring the absorbance of standard potassium chromate in 0.2M KOH solution. All measurements were carried out at the room temperature which was maintained at 25±0.5ºC. By following Ion- intermediate model pair, the dissociation constant was determined[8]:

$$pk_a = \frac{\left(\in_{app} - \in'\right)^2 f^2 C_t}{\left(\in_{In^-} - \in'\right)\left(\in_{In^-} - \in_{app}\right)}$$

It follows from above equation that a plot of $\in_{app.}$ vs. $\frac{\left(\in_{app.} - \in'\right)^2 f^2 C_t}{\left(\in_{In^-} - \in'\right)}$ at any wavelength will be a straight line and K_{HIn} will be given by the reciprocal of the slope.

RESULTS

Table 3 1a Spectrophotometry of Mixtures of 4-Amino benzoic acid (PABA) and Nitric Acid (HNO_3) in 5 weight% Butanol-Water Mixtures at 360nm and 400nm

Con. of PABA M × 10^4	Con. of HNO_3M	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{360} \times 10^4$	$\epsilon_{400} \times 10^4$
0.8294		0.150	0.043	0.1808	0.0518
1.5234		0.218	0.047	0.1431	0.0308
2.3628	0.2	0.302	0.052	0.1278	0.0220
3.3811		0.388	0.063	0.1147	0.0186
4.0705		0.464	0.069	0.1139	0.0169

Table 3 1b Spectrophotometry of Mixtures of 4-Aminobenzoic acid (PABA) and Nitric Acid (HNO_3) in 10 weight% Butanol-Water Mixtures at 360nm and 400nm

Con. of PABA M × 10^4	Con. of HNO_3M	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{360} \times 10^4$	$\epsilon_{400} \times 10^4$
0.8172		0.160	0.052	0.1957	0.0636
1.772		0.244	0.058	0.1376	0.0327
2.8143	0.2	0.314	0.065	0.1115	0.0230
3.4620		0.388	0.073	0.1120	0.0210
4.2941		0.475	0.078	0.1106	0.0181

Table 3 1c Spectrophotometry of Mixtures of PABA and Nitric Acid (HNO_3) in 20 weight% Butanol-Water Mixtures at 360nm and 400nm

Con. of PABA M × 10^4	Con. of HNO_3M	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{360} \times 10^4$	$\epsilon_{400} \times 10^4$
0.7586		0.120	0.050	0.1581	0.0659
1.4652		0.185	0.053	0.1262	0.0361
2.0083	0.2	0.247	0.060	0.1229	0.0298
3.0094		0.343	0.065	0.1139	0.0215
4.0229		0.433	0.074	0.1076	0.0183

Table 3 1 d Spectrophotometry of Mixtures of PABA and Nitric Acid (HNO_3) in 30 weight% Butanol-Water Mixtures at 360nm and 400nm

Con. of PABA M × 10^4	Con. of HNO_3M	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{360} \times 10^4$	$\epsilon_{400} \times 10^4$
0.4214		0.073	0.040	0.1732	0.0949
1.0180		0.161	0.050	0.1581	0.0491
2.0462	0.2	0.268	0.061	0.1309	0.0298
3.0841		0.363	0.063	0.1177	0.0204
4.2230		0.459	0.065	0.1086	0.0153

Table 3.1e Spectrophotometry of Mixtures of PABA and Nitric Acid (HNO_3) in 40 weight % 1-Butanol-Water Mixtures at 360nm and 400nm

Con. of PABA M × 10^4	Con. of HNO_3M	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{360} \times 10^4$	$\epsilon_{400} \times 10^4$
0.8146		0.133	0.049	0.1632	0.0601
1.7232		0.205	0.051	0.1189	0.0295
2.0467	0.2	0.253	0.056	0.1236	0.0273
3.2423		0.349	0.062	0.1076	0.0191
4.0932		0.443	0.069	0.1082	0.0168

Table 3.2a Spectrophotometry with potassium salt of PABA (K-PABA) in 5 weight% 1-Butanol- Water Mixtures at 360nm and 400nm:

Con. of K-PABA M × 10^5	Absorbance at wavelength 360nm	Absorbance at wavelength 400nm	$\epsilon_{In^-_{360}} \times 10^4$	$\epsilon_{In^-_{400}} \times 10^4$
0.5312	0.049	0.054		
1.0324	0.095	0.099		
2.0801	0.177	0.195	0.8978	0.9177
3.1020	0.260	0.298		
4.1500	0.342	0.382		

Table 3.2b Spectrophotometry with potassium salt of PABA (K-PABA) in 10 weight% Butanol- Water Mixtures at 360nm and 400nm:

Con. of K-PABA M × 10^5	Absorbance at wavelength 360nm	400nm	$\in_{In^-_{360}} \times 10^4$	$\in_{In^-_{400}} \times 10^4$
0.9270	0.078	0.083		
1.7940	0.162	0.178		
2.7413	0.250	0.271	0.9688	0.9573
3.7981	0.321	0.365		
4.7582	0.406	0.457		

Table 3.2c Spectrophotometry with potassium salt of PABA (K-PABA) in 20 weight% Butanol- Water Mixtures at 360nm and 400nm:

Con. of K-PABA M × 10^5	Absorbance at wavelength 360nm	400nm	$\in_{In^-_{360}} \times 10^4$	$\in_{In^-_{400}} \times 10^4$
0.8206	0.077	0.081		
1.3452	0.115	0.127		
2.0650	0.180	0.205	0.7243	0.8768
2.8708	0.265	0.280		
3.5386	0.336	0.355		

Table 3.2d Spectrophotometry with potassium salt of PABA (K-PABA) in 30 weight% Butanol- Water Mixtures at 360nm and 400nm

Con. of K-PABA M × 10^5	Absorbance at wavelength 360nm	400nm	$\in_{In^-_{400}} \times 10^4$	
0.7621	0.065	0.078		
1.7698	0.145	0.165		
2.9530	0.243	0.280	0.7938	0.8633
4.1152	0.342	0.385		
5.2884	0.448	0.503		

Table 3.2e Spectrophotometry with potassium salt of PABA (K-PABA) in 40 weight% Butanol- Water Mixtures at 360nm and 400nm

Con. of K-PABA M × 10^5	Absorbance at wavelength 360nm	400nm	$\in_{In^-_{360}} \times 10^4$	$\in_{In^-_{400}} \times 10^4$
0.7235	0.063	0.081		
1.1934	0.098	0.120		
2.0752	0.180	0.205	0.7448	0.8299
3.1341	0.270	0.310		
4.0654	0.352	0.402		

Table 3.3a Spectrophotometry with PABA in 5 weight% Butanol-Water Mixtures at 360 nm

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{360}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{360}} - \in'_{360})^2 \times C_t}{(\in_{In^-_{360}} - \in'_{360})}$
0.6583	0.060	0.9171	0.9999	0.0527
1.0028	0.087	0.8675	0.9999	0.0686
1.5701	0.140	0.8916	0.9999	0.1411
2.0046	0.165	0.8231	0.9999	0.1592
2.5821	0.218	0.8442	0.9999	0.1721
3.0069	0.242	0.8048	0.9999	0.1619

A′ = 0.564; $\in_{In^-_{360}} = 0.9177 \times 10^4$; $\in'_{360} = 0.1147 \times 10^4$

Table 3.3b Spectrophotometry with PABA in 10 weight% Butanol-Water Mixtures at 360 nm:

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{360}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{360}} - \in'_{360})^2 \times C_t}{(\in_{In^-_{360}} - \in'_{360})}$
0.7213	0.066	0.9150	0.9999	0.0544
1.0221	0.095	0.9294	0.9999	0.0721
1.7125	0.149	0.8701	0.9999	0.1216
2.0344	0.181	0.8896	0.9999	0.1543
2.7519	0.231	0.8394	0.9999	0.2132

A′ = 0.588; $\in_{In^-_{360}} = 0.9688 \times 10^4$; $\in'_{360} = 0.1120 \times 10^4$

Table 3.3c Spectrophotometry with PABA in 20 weight% Butanol-Water Mixtures at 360 nm

Concentration of PABA M × 10^5	$\in_{In^-_{360}} \times 10^4$ Absorbance A	$\in_{app_{360}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{360}} - \in'_{360})^2 \times C_t}{(\in_{In^-_{360}} - \in'_{360})}$
0.7448	0.069	0.9264	0.9999	0.0672
1.6092	0.133	0.8264	0.9999	0.1121
2.3648	0.198	0.8372	0.9999	0.1610
3.0298	0.260	0.8581	0.9999	0.2218
3.8749	0.321	0.8284	0.9999	0.2614
4.4298	0.375	0.8464	0.9999	0.3172

A′ = 0.676; $\in_{In^-_{360}} = 0.7243 \times 10^4$; $\in'_{360} = 0.1139 \times 10^4$

Table 3.3d Spectrophotometry with PABA in 30 weight% Butanol-Water Mixtures at 360 nm:

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{360}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{360}} - \in'_{360})^2 \times C_t}{(\in_{In^-_{360}} - \in'_{360})}$
0.8105	0.078	0.9623	0.99999	0.0846
1.2709	0.115	0.9048	0.9999	0.1173
1.5712	0.152	0.9674	0.9999	0.1504
2.1035	0.185	0.8794	0.9999	0.1752
2.8218	0.220	0.7796	0.9999	0.2234
2.9421	0.250	0.9483	0.9999	0.2615

A′ = 0.809; $\in_{In^-_{360}} = 0.7938 \times 10^4$; $\in'_{360} = 0.1177 \times 10^4$

Table 3.3e Spectrophotometry with PABA in 40weight % Butanol-Water Mixtures at 360 nm:

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{360}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{360}} - \in'_{360})^2 \times C_t}{(\in_{In^-_{360}} - \in'_{360})}$
0.8204	0.073	0.8898	0.9999	0.0734
1.7608	0.130	0.7383	0.9999	0.1152
2.0813	0.167	0.8023	0.9999	0.1405
2.5379	0.205	0.8077	0.9999	0.1633
3.0395	0.234	0.7698	0.9999	0.1840
3.5225	0.272	0.7721	0.9999	0.2124

A′ = 0.995; $\in_{In^-_{360}} = 0.7448 \times 10^4$; $\in'_{360} = 0.1189 \times 10^4$

Table 3.4a Spectrophotometry with PABA in 5 weight% Butanol-Water Mixtures at 400 nm:

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{400}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{400}} - \in'_{400})^2 \times C_t}{(\in_{In^-_{400}} - \in'_{400})}$
0.6771	0.062	0.9156	0.9999	0.0715
1.0024	0.090	0.8978	0.9999	0.0961
1.8701	0.143	0.7646	0.9999	0.1402
2.0053	0.168	0.8377	0.9999	0.1597
2.6741	0.220	0.8227	0.9999	0.2217
3.0054	0.245	0.8151	0.9999	0.2462

A′ = 0.564; $\in_{In^-_{400}} = 0.8978 \times 10^4$; $\in'_{400.0} = 0.0169 \times 10^4$

Table 3.4b Spectrophotometry with PABA in 10 weight% Butanol-Water Mixtures at 400 nm

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{400}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{400}} - \in'_{400})^2 \times C_t}{(\in_{In^-_{400}} - \in'_{400})}$
0.8123	0.068	0.8371	0.9999	0.0861
1.0323	0.097	0.9396	0.9999	0.0854
1.8124	0.154	0.8497	0.9999	0.1607
2.0354	0.189	0.9285	0.9999	0.1908
2.7429	0.240	0.8749	0.9999	0.2316
3.0241	0.269	0.8895	0.9999	0.2813

A′ = 0.588; $\in_{In^-_{400}} = 0.9573 \times 10^4$; $\in'_{400} = 0.0230 \times 10^4$

Table 3.4c Spectrophotometry with PABA in 20 weight% Butanol-Water Mixtures at 400 nm

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{400}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{400}} - \in'_{400})^2 \times C_t}{(\in_{In^-_{400}} - \in'_{400})}$
0.7639	0.070	0.9163	0.9999	0.0693
1.7099	0.135	0.7895	0.9999	0.1286
2.3459	0.201	0.8568	0.9999	0.1900
3.0299	0.264	0.8713	0.9999	0.2457
3.5749	0.329	0.9203	0.9999	0.3052
4.6297	0.379	0.8186	0.9999	0.3367

A′ = 0.676; $\in_{In^-_{400}} = 0.8768 \times 10^4$; $\in'_{400} = 0.0215 \times 10^4$

Table 3.4d Spectrophotometry with PABA in 30 weight% Butanol-Water Mixtures at 400 nm

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{400}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{400}} - \in'_{400})^2 \times C_t}{(\in_{In^-_{400}} - \in'_{400})}$
0.8506	0.081	0.9522	0.9999	0.0880
1.4608	0.118	0.8077	0.9999	0.1217
1.9813	0.155	0.7823	0.9999	0.1645
2.1015	0.189	0.8993	0.9999	0.1814
2.7421	0.224	0.8168	0.9999	0.2346
2.8431	0.256	0.9004	0.9999	0.2838

A′ = 0.809; $\in_{In^-_{400}} = 0.8633 \times 10^4$; $\in'_{400} = 0.0153 \times 10^4$

Table 3.4e Spectrophotometry with PABA in 40 weight% Butanol-Water Mixtures at 400 nm:

Concentration of PABA M × 10^5	Absorbance A	$\in_{app_{400}} \times 10^4$	f^2	$\frac{f^2(\in_{app_{400}} - \in'_{400})^2 \times C_t}{(\in_{In^-_{400}} - \in'_{400})}$
0.8401	0.075	0.8937	0.9999	0.0749
1.6408	0.133	0.8105	0.9999	0.1327
2. 0512	0.170	0.8287	0.9999	0.1487
2.5269	0.208	0.8231	0.9999	0.1765
3.0275	0.238	0.7861	0.9999	0.2249

A′ = 0.995; $\in_{In^-_{400}} = 0.8299 \times 10^4$; $\in'_{400} = 0.0601 \times 10^4$

Table 3.5 Summery of pk_a values of Para amino Benzoic Acid (PABA) in 1-Butanol-Water Mixtures at 360nm and 400nm

Weight% of Butanol	pK_a at 360nm	pK_a at 400nm
0	4.09 ≠	4.09 ≠
5	3.83	3.84
10	3.72	3.71
20	3.62	3.64
30	3.86	3.88
40	3.91	3.93

DISCUSSION

From Tables 3.3a, 3.3b, 3.3c, 3.3d, 3.3e at 360nm and 3.4a, 3.4b, 3.4c,3.4d, 3.4e at 400nm in different solvent compositions are shown. The values of pK_a of Para Amino Benzoic Acid in 5,10,20,30 and 40 wt. % have been given in table 3.5. The table of pK_a vs. wt.% of Butanol-water given shows that at first the pK_a values of Para Amino Benzoic Acid in Butanol-water mixtures decreases up to 20 wt.% of Butanol and then increases with the increase of Butanol content. An initial decrease in pK_a at lower alcohol/non-aqueous liquid region, the dispersive force is dominant over the electrostatic force caused by the lowering of dielectric constant and thereby an overall decrease in pK_a was observed up to 20 wt.% concentration of alcohol / non-aqueous component in the solvent mixture. In our case, the initial increase of the dissociation of the PABA upto 20 wt% butanol is a results of large preferential increase in solvation energy of the anion of PABA through London-dispersion interaction of the p molecules with the chromophoric nitrogen atom and the one amino groups of the PABA. After that composition range, the electrostatic force of attraction predominates over the dispersive force as a result of which pK_a increases with the increase of the concentration of the non – aqueous component of the binary solvent mixture.

CONCLUSION

This research work help to measure the dissolution study, dissociation constant of weak acid. The dissociation constant of weak acid will help in understanding the chemistry of weak acid in aqueous medium as well as provide information in the area of electrochemistry. Similarly this type of study helps us to understand the dissociation, solubility of drugs are weak acid in nature. The values of pKa and pH are especially important to understand solubility profile, absorption, distribution of drug and drug product. So, it should be mentioned here that this research work will helpful so greatly in the field of pre-formulation study, dissolution study, formulation & dosage form development and drug delivery of drugs are slightly weakly acidic in nature.

References

1. K.P. Alter, J.L. Molloy, E.D. Niemeyer.(2005). "Spectrophotometric Determination of the Dissociation Constant of an Acid-Base Indicator Using a Mathematical Deconvolution Technique". *J. Chem. Educ.* vol. *82* (11), pages 1682-1685
2. A. Niazi, A. Yazdanipour, J. Ghasemi,cM.Kubista,A.Sheyda, M. Alikhaha (2009). "Spectrophotometric Determination of the Dissociation Constants of Fluorescein in Micellar Media". *Croat. Chem. Acta vol.*82 (4), pages 753–759.
3. F. Tay ,M. Darun, S. Derirayak (2014). "A quantum chemical DFT/HF study on acidity constant of some benzothaizole & thaiazole derivatives". *Indian journal of chemistry*.vol 53B, pages 102-110.
4. S. M. Hossen, G. Akteruzzaman *et al* (2012). "Spectrophotometric Method for Determination of Dissociation Constant of weak acid like 2, 4-Dinitrophenol in 1-Propanol-Water Mixtures at 24.5±0.5ºC". Der Pharma Chemica, vol. 4(4) pages 1375-1384.
5. S. J. Raj, J. Subha, S. B.S. Alwar (2014). "Conductometric Studies On Sodium Acetate And Sodium Benzoate in Ethanol – Water Mixed Solvent Media" *International Journal of Advanced Chemical Science and Applications*, Vol.2(4),pages 44-49.
6. J.Ghasemi, H.Peyman, A Niazi (2007). "Spectrophotometric Determination of Acidity Constants of 4-(2-Pyridylazo) Resorcinol in Various Micellar Media Solutions". Journal of Chinese Chemical Society. Vol. 54((4), pages 1093–1097.
7. . Avdeef, K. J. Box, J. E. A Comer,M. Gilges, M. Hadley, C. Hibbert, W. Patterson and K. Y. Tam, *Journal of Pharmaceutical and Biomedical Analysis* 20(4), 1999,Pages 631-641
8. 8. Salah Chafaa, Jean Meullemeestre, Marie-José Schwing, François Vierling, olker Böhmer, Walter Vogt , Helvetica Chimica Acta. 76 (4), 1425-1434, (2004).