Compatibility and stability of analgesic admixtures for parenteral use: paracetamol, ketoprofen and tramadol

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The management of moderate post-operative pains is well relieved by the associations of several analgesic drugs as, paracetamol, ketoprofen and tramadol. These combinations improve post-operative analgesia and functional outcome after surgery. The admixture of these drugs for parenteral use would simplify the nursing care of patient; however this practice is forbidden by the technical documents of each drug.

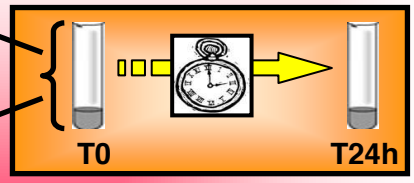
The aim of the study was to validate the compatibility and the stability of paracetamol, ketoprofen and tramadol admixtures for parenteral use.

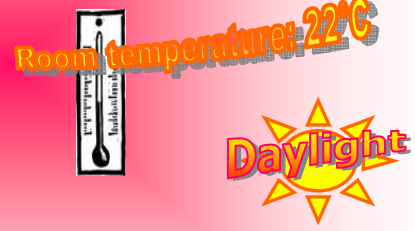
Design

- *Drugs*

Analgesic alone
Paracetamol (10 mg/mL)
Ketoprofen (1 mg/mL)
Tramadol (0,98 mg/mL)

Analgesic admixtures
1- Paracetamol (10 mg/mL)
Ketoprofen (1 mg/mL)
2- Paracetamol (10 mg/mL)
Tramadol (0,96 mg/mL)
3- Ketoprofen (0,98 mg/mL)
Tramadol (0,98 mg/mL)
4- Paracetamol (9,8 mg/mL)
Ketoprofen (0,98 mg/mL)
Tramadol (0,98 mg/mL)





- *Measures on each solution*

Liquid chromatography analysis
pH measure
Visual control

Results

Analgesic solutions alone

Time (min)		0	15	30	60	120	240	1440
Concentration		mg/ml	Percentage of initial concentration (%)					
Paracetamol	mean	9.64	100.4	99.7	99.5	99.4	99.9	98.6
10 mg/ml	sd	0.01	0.7	0.8	1.1	0.1	1.4	0.9
	n	3	3	3	3	3	3	3
pH		4.4	4.4	4.4	4.4	4.4	4.4	4.4
Visual control		-	-	-	-	-	-	-
Ketoprofen	mean	0.96	98.1	97.8	97.3	99.4	95.6	96.9
1 mg/ml	sd	0.02	0.4	4.7	1.4	0.4	1.3	2.7
	n	3	3	2	3	2	2	3
pH		5.8	5.8	5.8	5.8	5.8	5.8	5.8
Visual control		-	-	-	-	-	-	-
Tramadol	mean	0.89	99.1	100.1	100.3	99.9	102.3	102.1
0,98 mg/ml	sd	0.06	3.7	5.8	3.9	4.1	5.3	4.3
	n	2	3	3	3	3	3	3
pH		5.3	5.3	5.3	5.3	5.3	5.3	5.3
Visual control		-	-	-	-	-	-	-

Admixture of 3 analgesics

Time (min)		0	15	30	60	120	240	1440
Concentration		mg/ml	Percentage of intial concentration (%)					
Paracetamol	mean	10.04	98.8	101.5	101.6	100.5	98.3	98.2
9,8 mg/ml	sd	0.36	4.5	5.2	3.7	6.2	4.0	3.5
	n	7	7	7	6	8	8	7
Ketoprofen	mean	0.96	103.3	100.3	100.6	100.9	101.0	99.7
0,98 mg/ml	sd	0.01	7.4	1.0	1.1	1.3	1.8	2.1
	n	8	8	7	8	8	7	8
Tramadol	mean	0.96	102.2	99.4	97.3	98.1	98.6	97.9
0,98 mg/ml	sd	0.08	14.7	8.4	7.1	7.1	7.4	6.9
	n	8	8	8	8	8	8	8
pH		5	5	5	5	5	5	5
Visual control		-	-	-	-	-	-	-

Admixtures of 2 analgesics

Time (min)		0	15	30	60	120	240	1440
Concentration		mg/ml	Percentage of intial concentration (%)					
Paracetamol	mean	10.63	100.8	100.9	102.4	102.0	100.8	99.8
10 mg/ml	sd	0.43	3.1	3.6	4.5	4.7	3.7	5.1
	n	8	8	7	8	7	8	8
Ketoprofen	mean	1.00	98.1	98.8	98.0	101.8	98.4	97.5
1 mg/ml	sd	0.03	3.6	5.6	2.9	12.4	3.4	4.9
	n	8	8	8	8	8	8	8
pH		5	5	5	5	5	5	5
Visual control		-	-	-	-	-	-	-
Paracetamol	mean	9.44	101.3	108.4	104.2	101.5	103.8	96.5
9,8 mg/ml	sd	0.86	13.4	8.7	11.7	8.3%	13.6	13.6
	n	8	7	5	7	8	7	7
Tramadol	mean	0.94	96.4	102.0	99.7	99.9	97.3	100.9
0,98 mg/ml	sd	0.06	12.9	9.7	13.4	12.1	7.9	13.9
	n	8	8	8	7	8	6	7
pH		4.7	4.7	4.7	4.7	4.7	4.7	4.7
Visual control		-	-	-	-	-	-	-
Ketoprofen	mean	0.95	99.0	99.7	100.5	99.1	100.4	102.9
0,98 mg/ml	sd	0.02	0.8	1.1	5.1	1.1	1.7	10.2
	n	7	8	8	8	7	8	7
Tramadol	mean	0.97	99.9	103.0	98.9	96.8	97.5	96.%
0,98 mg/ml	sd	0.11	11.9	3.5	10.3	9.7	8.9	10.1
	n	8	8	8	8	8	8	7
pH		5.5	5.5	5.5	5.5	5.5	5.5	5.5
Visual control		-	-	-	-	-	-	-

NO
pH variation
Alteration of solution aspect
Concentration variation over 10%

Conclusion

According to the results of the present study, admixtures of paracetamol, ketoprofen and tramadol are compatible and stable. These admixtures would allow an efficient and safer treatment of moderate post-operative pains.