**SUPPLEMENTARY TABLES**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **30’** | **60’** | **120’** | **150’** | **180’** | **240’** | **300’** |
| MRP | 1±3,52Me=0 | 3,27±5,57Me=4,3 | 5,18±5,77Me=6,3 | 5,61±6,91Me=6,7 | 1,46±6,3Me=1 | -1,36±4,96Me=-1,1 | -0,07±2,4Me=0 |
| MRP + magnesium lactate micro | 11,6±5,71Me=12,5 | 25,88±5,36Me=27,6 | 33,31±7,4Me=33,3 | 28,51±5,4Me=30,4 | 24,77±4,81Me=25 | 24,71±8,39Me=25 | 3,09±7,98Me=0 |
| MRP + magnesium lactate normal | 4,37±4,34Me=4,15 | 13,52±6,51Me=14,5 | 19,3±5,05Me=20 | 16,88±7,2Me=16,65 | 14,02±7,74Me=11,3 | 0,53±0,83Me=0 | 2,17±3,22Me=0,8 |
| MRP + magnesium hydroaspartate micro | 18,5±7,89Me=17,85 | 16,72±5,28Me=17,85 | 19,77±7Me=16,4 | 14,92±7,6Me=14,3 | 22,17±5,92Me=21,8 | 4,75±4,31Me=5,35 | 0±0Me=0 |
| MRP + magnesium hydroaspartate normal | 12,77±5,2Me=12,7 | 12,17±5,19Me=10,9 | 15,8±3,24Me=16,4 | 9,72±5,65Me=7,1 | 11,57±5,59Me=9,1 | 2,47±3,02Me=1,85 | 0±2,34Me=0 |
| MRP + magnesium chloride micro | 11,8±4,72Me=12,9 | 25,08±4,73Me=24,1 | 29,49±5,2Me=30,4 | 27,34±4,8Me=25 | 22,91±4,7Me=24,5 | 22,17±9,59Me=18,8 | 1,14±5,37Me=0 |
| MRP + magnesium chloride normal | 10,98±5,1Me=10 | 19,2±5,88Me=20 | 24,6±5,17Me=25 | 23±4,94Me=21,3 | 21,8±3,2Me=21,3 | 20,18±5,17Me=20,7 | 0,03±2,09Me=0 |

**Table A. Descriptive statistics concerning the effect of magnesium salts (lactate, hydroaspartate, chloride) in micronized form (micro) and a normal form on the analgesic activity of morphine (MRP)**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **15’** | **30’** | **45’** | **60’** | **75’** | **90’** | **105’** |
| TRAM | 2,88±4,58Me=3,6 | -0,68±1,52Me=0 | -1,4±5,37Me=-3,4 | 0,72±1,61Me=0 | 1,44±1,97Me=0 | 0,7±3,9Me=0 | -0,72±1,6Me=0 |
| TRAM + magnesium lactate micro | 46,6±13,8Me=48,45 | 27,42±8,36Me=29,3 | 18,93±7,38Me=19,25 | 7,1±6,84Me=5,5 | 1,35±1,56Me=0,9 | 0,9±3Me=1,55 | -0,2±2,32Me=0 |
| TRAM + magnesium lactate normal | 23,77±7,22Me=25 | 17,17±7,08Me=14,3 | 6,87±1,74Me=7,1 | 3,28±3,63Me=3,65 | 1,53±2,44Me=0 | -0,28±2,91Me=0 | -0,3±1,77Me=0 |
| TRAM + magnesium hydroaspartate micro | 26,62±2,87Me=27,25 | 24,23±4,55Me=23,95 | 24,77±4,12Me=25,65 | 17,7±6,19Me=18,1 | 3,95±3,79Me=3,6 | 3,37±6,03Me=3,55 | 0,28±0,69Me=0 |
| TRAM + magnesium hydroaspartate normal | 11,9±6,2Me=14,3 | 10,73±6,9Me=8,9 | 5,21±4,14Me=5,35 | 5,2±2,5Me=5,35 | 2,75±1,54Me=3,6 | 0,95±2,28Me=0 | -0,9±1,5Me=0 |
| TRAM + magnesium chloride micro | 46,7±8,7Me=45,85 | 36,48±11,7Me=35,4 | 29,53±6,86Me=29,15 | 23,5±12,69Me=25 | 23,5±11,23Me=25 | 13,22±6,69Me=16,7 | 4,15±4,55Me=4,15 |
| TRAM + magnesium chloride normal | 36,48±6,15Me=38,55 | 33,68±6,24Me=33,3 | 34,7±5,68Me=33,3 | 27,08±9Me=29,15 | 21,55±5,53Me=20,85 | 18,75±8,22Me=16,7 | 5,55±3,38Me=6,25 |

**Table B. Descriptive statistics concerning the effect of magnesium salts (lactate, hydroaspartate, chloride) in micronized form (micro) and a normal form on the analgesic activity of tramadol (TRAM)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Compound** | **5’** | **15’** | **30’** | **45’** | **60’** | **90’** |
| OXC | 3,55±4,1Me=3,55 | 4,45±3,39Me=5,35 | 4,37±3,42Me=5,2 | -0,82±1,65Me=0 | -0,82±1,65Me=0 | 0±0Me=0 |
| OXC + magnesium lactate micro | 31,78±12,13Me=28,6 | 30,27±12,06Me=28,6 | 30,76±9,7Me=32,1 | 11,01±7,72Me=14,3 | 2,57±4,39Me=0 | -0,47±1,24Me=0 |
| OXC + magnesium lactate normal | 30,98±1,49Me=31 | 16,4±1,33Me=16,4 | 16,4±1,33Me=16,4 | 5,5±1,2Me=5,5 | 1,88±1,17Me=1,9 | 1,88±1,17Me=1,9 |
| OXC + magnesium hydroaspartate micro | 47,03±6,56Me=50 | 41,67±10,28Me=44,65 | 38,08±7,04Me=35,7 | 7,1±0Me=7,1 | 1,78±2,98Me=0 | 0,6±1,47Me=0 |
| OXC + magnesium hydroaspartate normal | 14,95±2,02Me=14,3 | 12,4±3,8Me=14,3 | 11,5±3,62Me=12,5 | 5,25±1,91Me=5,15 | 4,35±3,29Me=5,15 | -0,82±1,65Me=0 |
| OXC + magnesium chloride micro | 29,37±12,74Me=25 | 27,83±11,04Me=25 | 27,9±11,46Me=27,6 | 7,46±4,32Me=7,1 | -0,37±5,79Me=0 | -1,43±2,63Me=0 |
| OXC + magnesium chloride normal | 24,12±9,12Me=28,6 | 23,93±4,55Me=21,4 | 23,85±3,81Me=22,25 | 8,43±5,67Me=7,1 | 3,65±4Me=3,55 | -1,12±2,73Me=0 |

**Table C. Descriptive statistics concerning the effect of magnesium salts (lactate, hydroaspartate, chloride) in micronized form (micro) and a normal form on the analgesic activity of oxycodone (OXC)**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Day | MRP | MRP + magnesium lactate micro | MRP + magnesium lactate normal | OXC | OXC + magnesium lactate micro | OXC + magnesium lactate normal |
| 1 | 4,63±6,79Me=3,35 | -0,77±3,42Me=0 | 0,6±1,47Me=0 | -1,12±2,73Me=0 | 0±0Me=0 | -0,6±1,47Me=0 |
| 2 | 5,07±5,47Me=5 | 5,13±5,63Me=4,75 | 3,43±3,81Me=2,9 | -0,55±1,35Me=0 | 2,38±2,91Me=1,8 | 0±2,28Me=0 |
| 3 | 9±4,31Me=8,35 | 20,9±9,33Me=20,35 | 7,45±2,51Me=7,4 | -0,55±1,35Me=0 | 13,02±4,93Me=12,5 | 4,73±1,76Me=3,6 |
| 4 | 12,9±4,5Me=11,65 | 27,68±4,14Me=25,4 | 11,25±6,66Me=7,4 | 2,4±1,86Me=3,6 | 11,87±4,4Me=12,5 | 6,48±3,4Me=5,35 |
| 5 | 11,75±5,26Me=11,65 | 31,97±7,56Me=32,75 | 12,45±3,49Me=13,05 | 2,38±2,91Me=1,8 | 16,02±3,86Me=16,1 | 13,62±3,52Me=14,3 |
| 6 | 8,45±4,86Me=8,35 | 31,98±5,46Me=31,3 | 17,5±6,67Me=18,7 | 4,7±2,92Me=5,35 | 37,92±5,96Me=39,3 | 15,37±4,73Me=16,1 |
| 7 | 6,23±4,3Me=5 | 29,82±5,78Me=28,15 | 16,9±7,16Me=18,7 | 5,23±2,92Me=6,9 | 39,7±5,61Me=41,1 | 18,32±5,66Me=21,05 |
| 8 | 4,08±6,39Me=3,35 | 11,35±3,13Me=12 | 11,87±5,18Me=14,85 | 0,6±1,47Me=0 | 0,6±1,47Me=0 | 7,7±4,21Me=7,1 |
| 9 | -1,07±1,65Me=0 | -1,85±2,82Me=-0,8 | 0,1±4,68Me=0 | 0,6±1,47Me=0 | 0,6±1,47Me=0 | 2,95±2,67Me=3,5 |
| 10 | -0,52±2,44Me=0 | -1,32±1,54Me=-0,8 | -0,63±1,55Me=0 | -0,55±1,35Me=0 | -0,57±1,39Me=0 | 0,6±1,47Me=0 |

**Table D. Descriptive statistics concerning the effect of long-term administration of magnesium lactate in micronized form (micro) or normal form on the analgesic activity of morphine (MRP) and oxycodone (OXC)**

|  |  |  |  |
| --- | --- | --- | --- |
| **Day** | **TRAM** | **TRAM magnesium lactate micro** | **TRAM magnesium lactate normal** |
| 1 | 0,77±4,49Me=0 | 2,25±3,08Me=1 | 0,73±5,47Me=1,9 |
| 2 | 5,8±6,43Me=3,7 | 2,93±3,44Me=1,9 | 6,22±5,33Me=5,75 |
| 3 | 4,72±9,33Me=3,85 | 13,67±7,1Me=13,1 | 9,92±3,66Me=11,1 |
| 4 | 3,38±6,99Me=3,85 | 18,07±5,8Me=16,65 | 11,9±4,55Me=10,7 |
| 5 | 4,68±6,72Me=3,55 | 19,37±6,45Me=16,95 | 14,42±5,75Me=12,9 |
| 6 | 6,95±3,13Me=7,4 | 24,47±10Me=23,75 | 15,67±3,91Me=14,85 |
| 7 | 10,73±5,59Me=7,4 | 38,92±9,99Me=38,9 | 19,52±5,5Me=19,25 |
| 8 | 11,93±5,43Me=11 | 32,95±8,96Me=32,05 | 20,75±5,65Me=20,5 |
| 9 | 10,78±6,88Me=11,1 | 40,18±9,23Me=-37,75 | 18,88±4,64Me=19,25 |
| 10 | 10,78±6,09Me=9,3 | 37,68±11,02Me=-34,5 | 18,78±4,17Me=18,4 |
| 11 | 3,32±7,38Me=2 | 5,6±7,7Me=1,85 | 6,3±3,94Me=7,4 |
| 12 | 1,05±4,12Me=0 | -1,62±3,08Me=0 | -0,53±4,95Me=0 |

**Table E. Descriptive statistics concerning the effect of long-term administration of magnesium lactate in micronized form (micro) or normal form on the analgesic activity of tramadol (TRAM)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Compound** | **30’** | **45’** | **60’** | **120’** |
| Magnesium lactate normal 7,5 | 1,31±0,12Me=1,31 | 1,64±0,21Me=1,69 | 2,26±0,47Me=2,29 | 4,93±0,39Me=4,98 |
| Magnesium lactate micro 7,5 | 1,72±0,23Me=1,74 | 2,33±0,39Me=2,43 | 3,06±0,44Me=3,06 | 5,95±0,39Me=5,98 |
| Magnesium lactate normal 15 | 1,39±0,16Me=1,36 | 1,92±0,46Me=1,81 | 3,36±0,47Me=3,33 | 7,26±0,15Me=7,26 |
| Magnesium lactate micro 15 | 2,23±0,43Me=2,33 | 2,75±0,57Me=2,74 | 4,41±0,26Me=4,5 | 8,58±0,43Me=8,42 |
| Control | 0,49±0,14Me=0,47 | 0,62±0,21Me=0,63 | 0,86±0,14Me=0,88 | 0,99±0,11Me=0,98 |

**Table F. Descriptive statistics concerning the effect of magnesium lactate in normal and micronized forms at doses of 7.5 and 15 mg**

**kg-1 of magnesium ions kg-1 body mass on the concentration of ionized fraction of magnesium**