Package 'cpk'

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Title Clinical Pharmacokinetics

Description The package cpk provides simplified clinical pharmacokinetic functions for dose regimen design and modification at the point-of-care. Currently, the following functions are available: (1) ttc.fn for target therapeutic concentration, (2) dr.fn for dose rate, (3) di.fn for dosing interval, (4) dm.fn for maintenance dose, (5) bc.ttc.fn for back calculation, (6) ar.fn for accumulation ratio, (7) dpo.fn for orally administered dose, (8) cmax.fn for peak concentration, (9) css.fn for steady-state concentration, (10) cmin.fn for trough,(11) ct.fn for concentration-time predictions, (12) dlcmax.fn for calculating loading dose based on drug's maximum concentration, (13) dlar.fn for calculating loading dose based on drug's accumulation ratio, and (14) R0.fn for calculating drug infusion rate. Reference: Linares O, Linares A. Computational opioid prescribing: A novel application of clinical pharmacokinetics. J Pain Palliat Care Pharmacother 2011;25:125-135.

Depends R (>= 2.10.0)

License GPL-2

Disclaimer The authors take no responsibility for the outcome of therapy in any patient in which the techniques described in this package have been utilized.

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cpk-package *Clinical Pharmacokinetics.*

Description

This package was written to teach concepts and techniques to clinicians and pharmacists for individualizing drug therapy. While the package may be used by clinicians for actual dosage regimen analysis, design, and modification, caution should be exercised when applying the techniques described in R package cpk.

Details

Package:	cpk
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Author(s)

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References

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Linares OA, Daly D, Stefanovski D, Boston RC. A new model for using quantitative urine testing as a diagnostic tool for oxycodone treatment and compliance. J Pain Palliat Care Pharmacother 2013;27:(in press).

Examples

```
wtkg = 181;       # kg

# Drug Disposition Parameters
thalf = 4;        # h
ke    = 0.3180;   # h^-1
vd    = 4.5;      # L/kg
cl    = 1.43;     # L/h/kg
f     = 1.00;     # dpo range: 15-64% (avg 38%), IV f = 1.

#### Set TTC
ttc = 25;

#### Calculate dose rate (mg/h)
dr  <- dr.fn (ttc, cl, wtkg, f)

#### Set dosing interval based on thalf
di = 4;   # h

#### Calculate dose (if f = 1, dose IV)
dpo <- dpo.fn (dr, di)
```

```
dpo/1000 # convert to mg

#### Calculate loading dose based on cmax
cmax <- 18.93; vd <- 35;
dlcmax <- dlcmax.fn(cmax, vd)

#### Calculate loading dose based on ar
dm <- 276; ar <- 2.4;
dlar <- dlar.fn(dm, ar)

#-----------------------------------
# ANALYSIS
#-----------------------------------
bc.ttc <- bc.ttc.fn (dr, f, cl, wtkg)

#### predict avg steady-state concentration
# accumulation ratio
ar  <- ar.fn (ke, di)

css <- css.fn (f, dpo, di, cl, ar, wtkg)
css # mg/L

# predict fluctuation about steady-state (ug/L)
cmax <- cmax.fn (f, dpo, vd, ar, wtkg)
cmin <- cmin.fn (cmax, ke, di)

ct <- ct.fn(cmax, ke, time=0)
ct <- ct.fn(cmax, ke, time=4)

# infusion rate
css <- 14.43; cl <- 3.2;
R0  <- R0.fn(css, cl)
```

`ar.fn` *Accumulation ratio function*

Description

Calculates drug's accumulation ratio

Usage

```
ar.fn(ke, di)
```

Arguments

`ke`	Drug's total elimination rate constant ke (h^-1).
`di`	Dosing interval (h).

Value

Returns the calculated accumulation ratio

Author(s)

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Examples

```
ke <- 0.2350; di <- 4;
ar <- ar.fn(ke, di)
```

---

bc.ttc.fn *Back-calculation function*

Description

Performs a back-calculation to get the target therapeutic concentration (TTC) based on the administered dose.

Usage

```
bc.ttc.fn(dr, f, cl, wtkg)
```

Arguments

dr	dr is
f	bioavailability
cl	clearance rate
wtkg	weight in kg average man in US (NHANES III)

Value

Returns the back-calculated TTC (ug/L).

Author(s)

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References

See **cpk-package** help.

Examples

```
ttc <- 20; dr <- 2.26; cl <- 0.57; f <- 0.74; wtkg <- 86;
dr  <- dr.fn(ttc,cl,wtkg,f)
```

---

cmax.fn ***cmax** function*

Description

Calculates cmax (peak) drug concentration in ng/mL, which is the same as ug/mL.

Usage

```
cmax.fn(f, dpo, vd, ar, wtkg)
```

Arguments

f	is bioavailability.
dpo	is oral dose administered in ug.
vd	is apparent volume of distribution in L.
ar	is accumulation ratio.
wtkg	is patient weight in kg.

Value

Returns cmax ug/L.

Author(s)

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References

See **cpk-package** help.

Examples

```
f = 0.74; dpo <- 3440; vd = 2.8; ar = 2.4; wtkg=86;
cmax <- cmax.fn(f, dpo, vd, ar, wtkg)
```

cmin.fn *__cmin__ function*

Description

Calculates cmin (trough) drug concentration in ng/mL, which is the same as ug/mL.

Usage

```
cmin.fn(cmax, ke, di)
```

Arguments

cmax	is the maximum concentration of drug (peak level).
ke	Drug's total elimination rate constant.
di	is the dosing interval in h.

Value

Returns cmin ug/L.

Author(s)

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References

See **cpk-package** help.

Examples

```
cmax <- 25.37; ke <- 0.1333; di <- 4;
cmin <- cmin.fn(cmax, ke, di)
```

css.fn *__css__ function*

Description

Calculates css (steady-state) drug concentration in ng/mL, which is the same as ug/mL.

Usage

```
css.fn(f, dpo, di, cl, ar, wtkg)
```

Arguments

f	is bioavailability.
dpo	is oral dose administered in ug.
di	is the dosing interval in h.
cl	is the total clearance rate in L/kg/h.
ar	is stepwise accumulation ratio.
wtkg	is patient weight in kg.

Value

Returns css in mg/L and ug/L

Author(s)

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References

See **cpk-package** help.

Examples

```
f <- 0.74; dpo <- 3440; di <- 4; cl <- 0.37; ar <-1.4; wtkg <- 86;
css <-css.fn(f, dpo, di, cl, ar, wtkg)
```

---

ct.fn *ct function*

Description

Predicts drug concentration at specified time (default time=0 h) [ng/mL].

Usage

```
ct.fn(cmax, ke, time=0)
```

Arguments

cmax	is the maximum concentration (cmax).
ke	is the first-order elimination rate constant (ke).
time	is the time on the clearance curve for which a drug concentration is desired.

Value

Returns the concentration at specified time.

Author(s)

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References

See **cpk-package** help.

Examples

```
cmax <- 15; ke <- 0.1333; time <- 4;
ct <- ct.fn(cmax, ke, time=0)
```

---

di.fn *di function*

Description

Calculates a drug's dosing interval.

Usage

```
di.fn(msc, mec, ke)
```

Arguments

msc	Drug's maximum safe concentration or Cmax (peak) concentration.
mec	Drug's minimum effective concentration or Cmin (trough) concentration.
ke	Drug's total elimination rate constant.

Value

Returns the dosing interval (h).

Author(s)

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References

See **cpk-package** help.

Examples

```
msc <- 50; mec <- 20; ke <- 0.2078;
di  <- di.fn(msc, mec, ke)
```

dlar.fn *Loading dose function*

Description

Calculates a drug's loading dose based on its accumulation ratio

Usage

```
dlar.fn(dm, ar)
```

Arguments

dm	Drug's maintenance dose.
ar	Drug's accumulation ratio.

Value

Returns the calculated loading dose

Author(s)

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Examples

```
dm <- 276; ar <- 2.4;
dlar <- dlar.fn(dm, ar)
```

dlcmax.fn *Loading dose function*

Description

Calculates a drug's loading dose based on its cmax

Usage

```
dlcmax.fn(cmax, vd)
```

Arguments

cmax	Drug's maximum concentration (cmax).
vd	Drug's apparent volume of distribution (vd).

Value

Returns the calculated loading dose

Author(s)

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Examples

```
cmax <- 18.93; vd <- 35;
dlcmax <- dlcmax.fn(cmax, vd)
```

---

dm.fn *dm function*

Description

Calculates drug's maintenance dose.

Usage

```
dm.fn(dr, di)
```

Arguments

dr	is the dose rate.
di	is the dosing interval, which can be either computed or assigned (e.g., di <- 4)

Value

Returns the maintenance dose.

Author(s)

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References

See **cpk-package** help.

Examples

```
dr <- 1.42; di <- 4;
dm <- dm.fn(dr, di)
```

dpo.fn *dpo function*

Description

Calculates the oral dose of drug to give.

Usage

```
dpo.fn(dr, di)
```

Arguments

dr	is the dose rate in mg/h.
di	is the dosing interval in h.

Value

Returns oral dose administered in ug.

Author(s)

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References

See **cpk-package** help.

Examples

```
dr <- 0.86; di <- 4;
dpo <- dpo.fn(dr, di)
```

dr.fn *dr function*

Description

Calculates dose rate (mg/h).

Usage

```
dr.fn(ttc, cl, wtkg, f)
```

Arguments

ttc	target therapeutic concentration.
cl	clearance rate.
wtkg	patient's weight in kilograms.
f	bioavailability.

Value

Returns the dose rate.

Author(s)

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References

See **cpk-package** help.

Examples

```
ttc <- 32.74; cl <- 0.59; wtkg <- 86; f <- 0.74;
dr <- dr.fn(ttc, cl, wtkg, f)
```

R0.fn *R0 function*

Description

Predicts drug infusion rate [ug/h].

Usage

```
R0.fn(css, cl)
```

Arguments

css	is the steady-state concentration.
cl	is the clearance rate.

Value

Returns the infusion rate.

Author(s)

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References

See **cpk-package** help.

Examples

```
css <- 14.43; cl <- 3.2;
R0  <- R0.fn(css, cl)
```

---

ttc.fn *ttc function*

Description

Calculates a drug's target therapeutic concentration (ttc) based on its msc or cmax and mec or cmin in ng/mL, which is the same as ug/mL.

Usage

```
ttc.fn(msc, mec)
```

Arguments

msc	maximum safe concentration or cmax
mec	minimum effective concentration of cmin

Value

Returns target therapeutic concentration (ttc).

Author(s)

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References

See **cpk-package** help.

Examples

```
msc = 50; mec = 20;
ttc <- ttc.fn(msc, mec)
```

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