

Lithium als Antidepressivum

(Bateman-Funktion)

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Der zeitliche Verlauf der Wirkstoffwirkung als Simulation mit den pharmakokinetischen Angaben des Medikaments Lithium¹. Das Datenblatt enthält folgende Angaben:

1 Indications

In 1843 Alexander Ure introduced lithium into modern medicine². *Lithium* is indicated for the prophylaxis and treatment of mania, manic depression and depression.

Actions

Lithium carbonate (Li_2CO_3) provides a source of lithium ions (Li^+) that may act by competing with sodium ions (Na^+) at various sites in the body. Therapeutic concentrations of lithium have almost no discernible psychotropic effects in normal volunteers but considerable effect in patients suffering from affective disorders. The mechanism of action is unknown.

2 Pharmacokinetics

Lithium ions are almost completely absorbed from the gastrointestinal tract, complete absorption occurring after about 8 hours. **Peak plasma concentrations occur after about 2-4 hours**. Lithium initially distributes into extracellular fluid and then to most other tissues. The final volume of distribution equals that of total body water.

Lithium slowly enters cerebrospinal fluid achieving at steady state 40% of the plasma concentration. Elimination occurs via the kidneys but lithium can also be detected in sweat

¹ Informations for Health Professionals, Data Sheet,

<http://www.medsafe.govt.nz/profs/Datasheet/1/Lithiumcarbonatecap.htm>

² Mohandas E, Rajmohan V. Lithium use in special populations. Indian J Psychiatry 2007;49:211-8

and saliva. *The biological half-life is variable ranging from 7-20 hours* and may be longer at night. Poor renal function impairs excretion.

Lithium is able to cross the placenta and is excreted in breast milk.

The usual dose for prophylactic therapy is 0.25g-1.5g daily. Dosage needs to be adjusted according to the results of serum-lithium estimations obtained under strictly controlled conditions. Such estimations should be made weekly at first then, once consistent concentrations are achieved, monthly or two monthly tests may be made.

Lithium carbonate 250 mg per capsule

3 Simulation³

3.1 Simulationsdiagramm (Typ 4)⁴

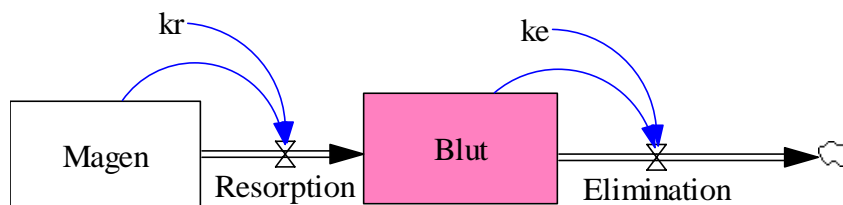


Abbildung 1: Simulationsdiagramm der Aufnahme von Lithium ins Blut

3.2 Zeitdiagramm

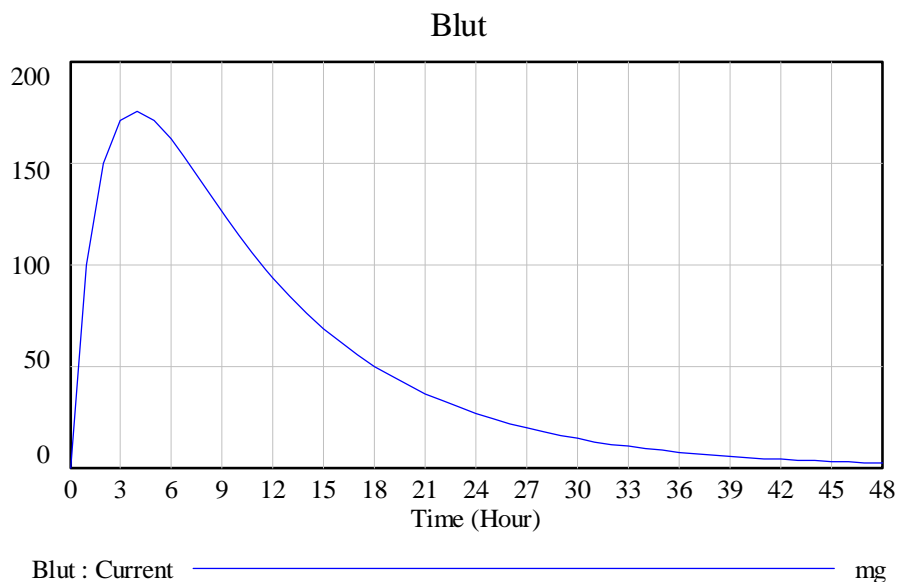


Abbildung 2: Zeitdiagramm der Lithiummenge im Blut

Interpretation

³ Software: Programm Vensim® PLE, Ventana Systems, Inc.

⁴ Bützer Peter, Roth Markus, Die Zeit im Griff, verlag pestalozzianum, Zürich 2006, 57ff

Der Verlauf dieser Menge im Blut entspricht gemessenen Werten⁵.

4 Der Durchgang durch die Blut-Hirn-Schranke

Nachbildung von: Lithium slowly enters *cerebrospinal fluid* achieving at steady state 40% of the plasma concentration.

4.1 Simulationsdiagramm (Typ 3 und Typ 4)⁶

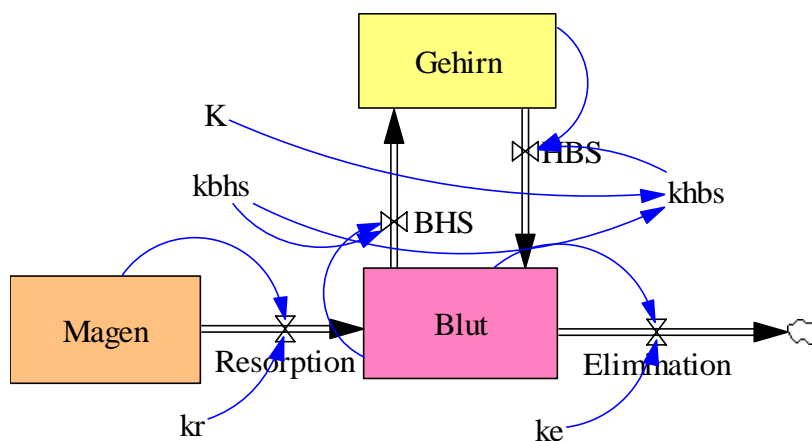


Abbildung 3: Simulationsdiagramm der Lithiumaufnahme ins Blut und dessen Verteilung im Gehirn

K ca. 1 (ist nicht sehr relevant, siehe Simulation)

$kbhs = 0.015$ (notwendig, damit die 40% der Blutkonz. erreicht werden)

$khbs = kbhs/K$ (aus Gleichgewicht)

4.2 Dokumentation (Gleichungen, Parameter)

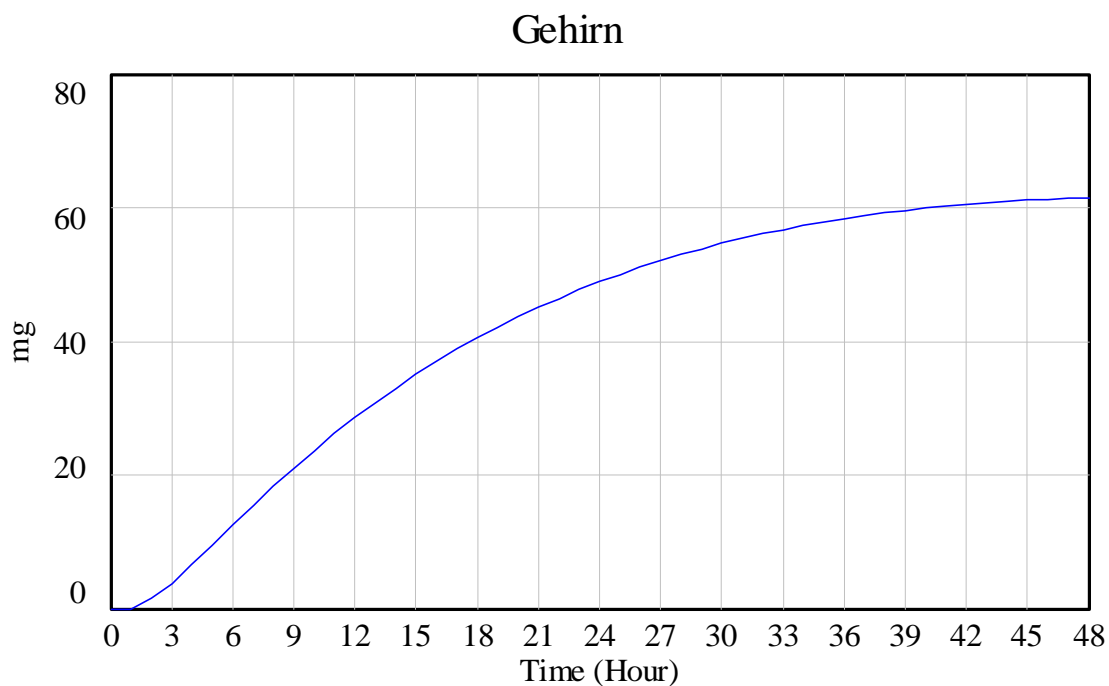
- (01) $BHS = kbhs * Blut$
Units: mg/Hour [0,?]
- (02) $Blut = INTEG (+Resorption - Elimination - BHS + HBS, 0)$
Units: mg
- (03) $Elimination = ke * Blut$
Units: mg/Hour
- (04) $FINAL TIME = 48$
Units: Hour
The final time for the simulation.
- (05) $Gehirn = INTEG (BHS - HBS, 0)$
Units: mg [0,?]
- (06) $HBS = khbs * Gehirn$
Units: mg/Hour [0,?]

⁵ Emami Jaber, Tavakoli Naser, Movahedian Ahmad, Formulation of sustained - release lithium carbonate matrix tablets: influence of hydrophilic materials on the release rate and in vitro-in vivo evaluation, J Pharm Pharmaceut Sci (www.ualberta.ca/~csps) 7(3):338-344, 2004

⁶ Bützer Peter, Roth Markus, Die Zeit im Griff, Systemdynamik in Chemie und Biochemie, verlag pestalozzianum, Zürich 2006, S. 50ff, 57ff

- (07) INITIAL TIME = 0
Units: Hour
The initial time for the simulation.
- (08) K= 1
Units: Dmnl [0,10]
- (09) kbhs= 0.015
Units: 1/Hour [0,0.1]
- (10) ke= 0.02
Units: 1/Hour [0.01,0.0347]
- (11) khbs= kbhs/K
Units: 1/Hour [0,?]
- (12) kr= 0.4
Units: 1/Hour [0.346,0.7]
- (13) Magen= INTEG (-Resorption, 250)
Units: mg
- (14) Resorption= kr*Magen
Units: mg/Hour
- (15) SAVEPER = TIME STEP
Units: Hour [0,?]
The frequency with which output is stored.
- (16) TIME STEP = 1
Units: Hour [0,?]
The time step for the simulation.

4.3 Zeitdiagramm



Gehirn : Current

Abbildung 4: Zeitdiagramm der Lithiummenge im Gehirn

4.4 Folgerung

Es zeigt sich der im Datenblatt für das Gehirn erwähnte Steady State!!