### **Supplementary *Table 1*** - Reactions and transporters in human caffeine metabolism and kinetic parameters.

|  |  |  |
| --- | --- | --- |
| Id | Information | Kinetics |
| **CAFT** | **Caffeine transport**  caffeine (disse) ↔ caffeine (cytosol)  Mechanism  TCDB:2.A.1.1 (glucose transporter subfamily)  Protein/Structure  UniProt:P11168 (GTR2\_HUMAN)  Gene  SLC2A2, GLUT2  Disease  OcMIM:227810 (Fanconi-Bickel syndrome; FBS) | **km(D-glc)=21.7 ± 1.8mM** (rat liver) ([Ciaraldi, et al., 1986](#_ENREF_6))  **km(D-glc)=66±14mM** (rat hepatocytes) ([Elliott and Craik, 1982](#_ENREF_12))  **km(D-glc)=17mM** (perfused rat liver, cited) ([Elliott and Craik, 1982](#_ENREF_12))  **km(D-glc)=30mM** (rat hepatocytes, cited) ([Elliott and Craik, 1982](#_ENREF_12))  km(3-O-MG)=42.3±4.1mM (human liver) ([Gould, et al., 1991](#_ENREF_17); [Walmsley, et al., 1998](#_ENREF_43))  km(3-O-Methyl glc)=17.3 **±** 4.3mM (rat liver) ([Ciaraldi, et al., 1986](#_ENREF_6))  **Vmax(D-glc)=220±19**mmol/min/l of cell H2O (rat hepatocytes) ([Elliott and Craik, 1982](#_ENREF_12))  **Vmax(D-glc)=345**mmol/min/l of cell H2O (perfused rat liver, cited) ([Elliott and Craik, 1982](#_ENREF_12))  **Vmax(D-glc)=70**mmol/min/l of cell H2O (rat hepatocytes, cited) ([Elliott and Craik, 1982](#_ENREF_12))  **km(D-gal)=174±48mM** (rat hepatocytes) ([Elliott and Craik, 1982](#_ENREF_12))  **km(D-gal)=100mM** (rat hepatocytes, cited) ([Elliott and Craik, 1982](#_ENREF_12))  **km(D-gal)>50mM** (GLUT2 enderocytes) ([Walmsley, et al., 1998](#_ENREF_43))  **km(D-gal)=85.5 ± 10.7mM** (human, liver-type GLUT2) ([Colville, et al., 1993](#_ENREF_7))  **km(D-gal)=92 ± 8.4mM** (human, liver-type GLUT2) ([Arbuckle, et al., 1996](#_ENREF_2))  **km(D-gal)~27.7mM** (dog liver, multiple indicator dilution curves ([Goresky, et al., 1973](#_ENREF_16))  **Vmax (D-gal)=288±48** mmol/min/l of cell H2O (rat hepatocytes) ([Elliott and Craik, 1982](#_ENREF_12))  **Vmax (D-gal)=160**mmol/min/l of cell H2O (rat hepatocytes, cited) ([Elliott and Craik, 1982](#_ENREF_12)) |
| **GALK** | **Galactokinase**  1,7-dimethylxanthine + S-adenosyl-L-methionine ↔ S-adenosyl-L-homocysteine + caffeine + H(+)  **Reaction**  EC:2.1.1.160  RHEA:10283  KEGG:R07921  MetaCyc:RXN-7601  Protein  [UniProt:P51570](http://www.uniprot.org/uniprot/P51570)(GALK1\_HUMAN)  homodimer P51570\*2  **Gene**  GALK, GALK1  Disease  [MIM:230200](http://www.omim.org/entry/230200) (GALCT2 Galactosemia II)  Galactokinase being rate limiting for galactose clearance ([Schirmer, et al., 1986](#_ENREF_34)) | **Two-substrate ordered, ternary complex reaction** ([Timson and Reece, 2003](#_ENREF_41))  **kcat(gal) = 8.7±5 1/s** (SABIORK:14785)([Timson and Reece, 2003](#_ENREF_41))  **km(atp) = 0.034±0.004mM** (SABIORK:14792)([Timson and Reece, 2003](#_ENREF_41))  **km(atp) = 0.12mM** (adult, rat liver){Cuatrecasas1965}  **km(gal)=0.97±0.22mM** (SABIORK:14785) ([Timson and Reece, 2003](#_ENREF_41))  **km(gal) = 0.436mM** (SABIORK:45367), ([Sangiuolo, et al., 2004](#_ENREF_33))  **km(gal) = 0.15mM** (adult, rat liver){Cuatrecasas1965}  km(gal) = 0.65mM (newborn, rat liver){Cuatrecasas1965}  km(gal) = 0.91mM (18 day fetal, rat liver){Cuatrecasas1965}  **km(gal) = 0.14±0.01mM** (SEM, N=6, adult rat liver) {Walker1968}  km(gal) = 0.15±0.01mM (SEM, N=4, neonatal rat liver) {Walker1968}  km(gal) = 0.14±0.01mM (SEM, N=4, foetal rat liver) {Walker1968}  **Uncompetitive product inhibition** of GALK (adult rat liver) by gal1p with both 1mM and 5mM gal1p altering the Km for galactose from 0.150mM to 0.800mM (1mM gal1p caused 15% inhibition, 5mM gal1p 50% inhibition)  **ki(gal1p) = 5.3mM (5.0-5.7mM)** (adult rat liver) ([Cuatrecasas and Segal, 1965](#_ENREF_10))  **km(gal)<0.83mM** (dog liver, multiple indicator dilution curves) ([Goresky, et al., 1973](#_ENREF_16)) |

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