Of homo, mus and rattus

by Jim Duke, PhD

Jim Duke

James Duke received his PhD in Botany from the University of North Carolina, moving on to postdoctoral studies at Washington UNiversity and the Missouri Botanical Garden in St. Louis where assumed professor and curator duties, respectively. Dr. Duke spends a signficant amount of his time exploring the ecology and culture of the Amazonian Rain Forest. In addition to a distinguished 30-year career with the United States Department of Agriculture, Dr. Duke sits on the board of directors and advisory councils of numerous organizations involved in plant medicine and the rainforest. He is also an accomplished musician, poet, and songwriter.

Three days before Valentine, February 1 2003,?I was snowed in and listening to local radio show, as I compiled away my nefarious reductionsitic database, nothing more than a weird selective indto a certain subset of the literature thas crossed my desk over a few decades. What should I hear but a Gary Null radishow and a?Null Hypothesis that caf feine poses a very serious health risk. my surprise, my small LD50 compilation below certainly hints that caffeine is dangerous, at least to rats, often 10 t(sometimes more than 30 times as toxic) as those essential oils so often used i aromatherapy. I know that rat LD50s don't equate to human LD50s, but find interesting that the oral LD50 of caffein rats (192 mg/kg) is the same as the LDlo (lowest lethal dose) in humans (a192 mg/kg). This suggests to lazy me that I can think of the oral LD50 in ra close to the LDlo for humans; I think t might at least put me in the right ball(order of magnitude). And for my 100 kg frame, I can extrapolate, very roughly, my LD50 by dividing a mouse LD50 (mg/kg) by ~ 7, a rat LD50?(in mg/kg) by?~ 4,

Granted, my database owes a whole lot to a whole lot of rats who died in the LD50 prov ings. I shan't apologi for past sins of the rodenticidal scientist who extinguished these rats in the inte ests of science. But their sacrifice makes me a bit better able t extrapolate LD50 val ues to humans. And even if we share ~99%

(See table 1)

All except the Divide By Column Above were derived, with permission from Boik. I lazily devised the divisor device (last column; divide by) to calculate dosages for humans; I think t Boik makes some interesting generalizations in discussing his generally recognized allometric approach.??A small animal, in general, will metabolize and excrete drugs quicker than a human. For this reason, the effective dose (ED) (and

Table 1: Conversion ratios, Animal to Human
[ED & LD] (After Boik, 2001)

Animal	Weight (KG)	Food G/Day	Man to Mammal Ratio	Divide by
Mouse	0.025	3	7.3:1	7
Hamster	0.125	15	4.9:1	5
Rat	0.2	15	4.3:1	4
Guinea Pig	0.5	30	3.4:1	3.5
Rabbit	2	60	2.4:1	2.5
Dog	10	250	1.6:1	1.5
Standard Man	70			

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for this paper, lethal dose; LD) (per kilo gram body weight) in an animal will be greater than that for a human. Boik cau tions that a compound found effective in animals would not necessarily be so in humans.

I often use caffeine as an example. The oral rat LD50=192 mg/kg can be extrap olated to oral Jim Duke LD50, roughly, dividing by 4 = 48 mg/kg. OR, going exactly with the Boik formula, 192 divid ed by 61.7 =3.111 g for a 70 kg standard man, or 44 mg/kg.

Even reports of LD50 dosages may vary ten-fold. The reports for oral caffeine LD50s in mice range from?127 to 1,200 mg/kg orl mus. Using the Duke divisor of 7, we get an extrapolation of 18-171 mg/kg per Jim Duke. Using the allometric formula, we get?1.2-11.5g caffeine per 70 kg human, which translates to 17-164 mg/kg for a 70 kilo standard man. Simon Mills in lectures at the Tai Sophia sug gests that humans vary 8-fold in their reactions to medicines. Seems to be true of mice and men. [I have heard that much greater variations occur, even with caf feine.]

Re: effective doses, compounds active in vitro at concentrations of 50 uM or less have good potential to be useful in vivo when they are used in synergistic con centrations.??Research papers often use ug/ml. or mg/ml instead of uM or mM. To convert ug/ml to uM, multiply by 1,000 and divide by the molecular weight, as found for example in the Merck Index.

While, I still don't have the data to prov it, I personally suspect that the isolated phytochemical, out of context, is more liable to generate side effects than the same phytochemical in its normal, genet ically familar context.?To my surprise, Steve Dentali sent me data sug gesting that iso-