DRUG AND CHEMICAL TOXICOLOGY
Vol. 26, No. 1, pp. 53-60, 2003

CalcDose: A Software for Drug Dosage Conversion Using Metabolically Active Mass of Animals

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ABSTRACT

This Visual Basic computer program has been developed for drug dosage conversions using metabolically active mass (MAM) of the animals. The two body weights (one with known dosage and the other, for which the dosage has to be calculated) and the known dosage are entered in the respective input boxes and the appropriate units are selected using the option buttons. The program displays the report in the form of both the animals' body weights and the respective dosages in milligram per kilogram body weight as well as the total actual doses in milligrams. The object oriented layout, flexible data entry and comprehensive report format render the *CalcDose* software a convenient and handy tool for dosage conversions.

INTRODUCTION

It is commonly observed that small animals have to be administered large dosages (per kilogram body weight) as compared to big animals or humans to achieve similar pharmacological effects. For instance, about five-fold higher dosages of prednisolone (3,6) and caffeine (8,13) have been reported for rats as compared to humans. Dosages of other drugs including cyclosporin (18,29), selegiline (1,24), melatonin (12,22), haloperidol (10,17), gentamicin (9,21), and dexamethasone (14,15) show similar trend. These variations occur due to varying metabolic activities of different animals. Although body weight varies from animal to animal across and within species, there is a remarkable consistency of the daily expenditure of energy expressed per metabolically active mass (MAM). About 20-30% of the whole body mass constitute fat material, which is metabolically inactive. On the other hand, the lean body mass (about 75% of body weight) contains all the body protein which takes part in maintaining homeostasis and is metabolically active. MAM is equal to body weight raised to 0.75 power, and holds true for freely feeding animals of different species as well as animals within a species. Although, in most of the pharmacological studies, the dosage of a drug is usually expressed in terms of milligram per kilogram (mg/kg) body weight, few investigators have also used less common but more realistic terms like mg/kg MAM (5,11) or mg/m^2 body surface area (BSA) (7,25).

Pharmacologists often face the problem of finding an optimum reference dosage to start with, for their initial pilot studies. A suitable dosage conversion has to be performed, if the dosage of a drug for the same species is unknown but for a totally different species is known to experimenter. There are two important methods for dosage conversions, based on BSA or MAM calculations, and provide a more

accurate cross-species comparison of activity and toxicity of various drugs (28). Several BSA based programs are accessible online for drug dosage conversions (26,27). These programs are suitable for human studies only, as one of the input parameters is height, which is difficult to measure in case of small animals and perhaps there is no established criteria for this purpose. The present software has been designed for dosage conversions between animals and humans, and is based on MAM measurements.

PROGRAM DESCRIPTION

The *CalcDose* software has been developed in Visual Basic 6.0 and would run in Windows environment as an executable file (32 KB). Briefly, there are two forms in the program; form 1 is the input form (Fig. 1) and form 2 is the result window (Fig. 2). There are 3 input boxes and 3 pairs of respective option buttons on form 1. The user has to input body weight of the animal in grams (suitable for small animal) or in kilograms (suitable for human) and the known dosage of the drug either in mg/kg or in milligrams (total dose for that body weight), whichever is known. Then the user enters the body weight of the animal for which the dosage has to be calculated. This entry enables the 'Calculate' command button, which was disabled at the start-up. When the 'Calculate' button is clicked, the result window appears showing the respective doses (mg) as well as dosages (mg/kg) for both the body weights. When the 'Next' button is clicked, the program prompts for next calculation, whereas the 'Print' and 'Exit' buttons can be used for printing the results and ending the program respectively.

SOFTWARE VALIDATION

The application of *CalcDose* software was validated using 8 selected drugs including cyclosporin, caffeine, selegiline, melatonin, haloperidol, gentamicin, prednisolone, and dexamethasone. The software was used to calculate dosages of these drugs for

Table 1. Validation of *CalcDose* software using reported dosages of various drugs.

Drug	Reported dosage mg/kg (Ref.)		Calculated dosage, mg/kg for rat using *CalcDose*[a]	% difference from reported dosage for rat	
	Human	Rat		Conversion based on BW	Conversion based on MAM[b]
Cyclosporin	3 (18)	20 (29)	17.40	85	13
Caffeine	4 (13)	20 (8)	23.19	80	15.9
Selegiline	0.107 (24)	0.5 (1)	0.62	78.6	24
Melatonin	0.07 (22)	0.5 (12)	0.41	86	18
Haloperidol	0.33 (10)	2 (17)	1.91	83.5	4.3
Gentamicin	3 (21)	20 (9)	17.40	85	13
Prednisolone	1 (3)	5 (6)	5.79	80	15.8
Dexamethasone	0.286 (15)	1.5 (14)	1.65	80.9	10

[a] Reported human dose was used to calculate appropriate dosage for rat.
[b] Method used in *CalcDose* software.
Abbreviations are: BW, body weight; MAM, metabolically active mass.

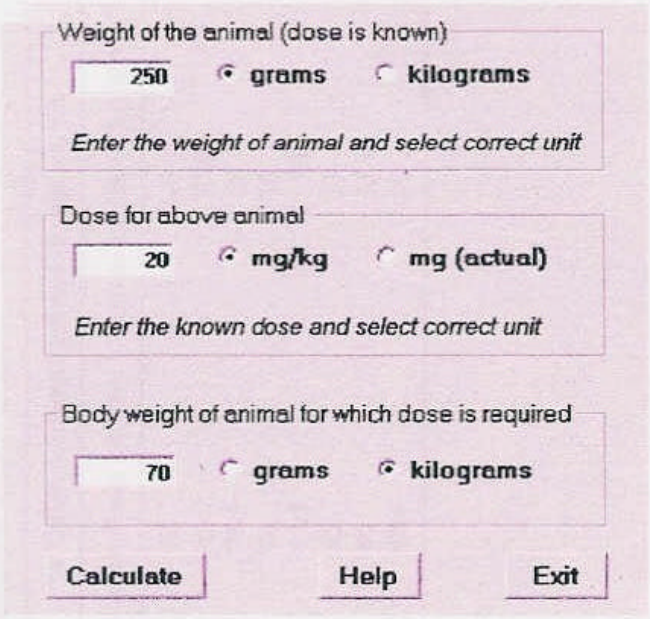

Figure 1. Input window: showing enteries for the calculation of a human equivalent dose using the know animal dosage (20 mg/kg for rat).

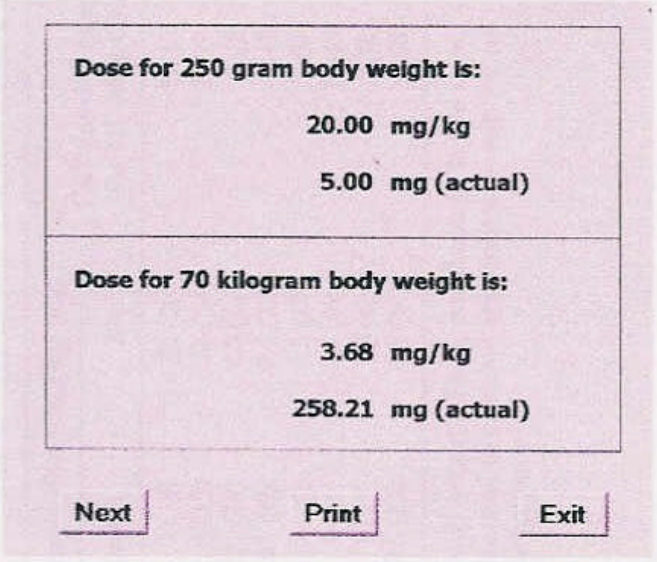

Figure 2. Report window: showing a representative print-out of results.

rats using the reported human dosages. The results following drug dosage conversions were compared with the reported dosages of these drugs for rats (Table 1). The mean percent variation was found to be significantly less (14.25±2.04 versus 82.37±1.00, P<0.001, Student's t-test) with MAM based procedure (*CalcDose* software). A comparative view of dosage conversion using direct actual body weights and MAM is shown in Fig. 3.

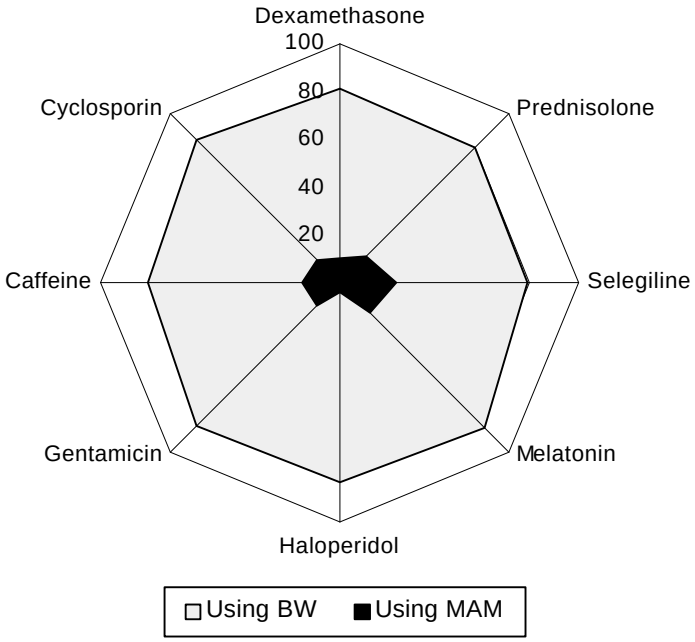

Fig. 3. Comparative view of dose conversion using actual body weight (BW) and metabolically active mass (MAM) of animals. Reported human dosages for 8 drugs were used to calculate appropriate dosages for rats. The shaded areas indicate the percent variations from the reported dosages while using BW (light shaded) or MAM (dark shaded) procedures. *CalcDose* program was used for MAM procedure.

DISCUSSION AND CONCLUSION

The findings of software validation clearly indicate that MAM based computations which are used in *CalcDose* program are fairly valid for dosage conversion between human and small animals. It is also indicative that several investigators prefer to express the doses of drugs in terms of human equivalents, in their animal studies to highlight their relevance to therapeutic importance (16,19), diagnostic value (20) or environmental concern (2,4,23). *CalcDose* software can be effectively used to calculate human equivalent dose of a drug tested in experimental animal. The main features of the program are optimal simplicity and flexibility of data input and a comprehensive report format. In pharmacological studies, body weight of experimental animals is exclusively expressed in grams or kilograms, which can be directly selected using the option buttons on the input form (Fig. 1) rendering the program more time-efficient. The results output window not only shows the intended dose calculation, instead comprised of the body weight of both the animals and their respective mg/kg and actual doses. Thus, if any doubt or discrepancy is impended in

results, the user can countercheck the data entry by viewing the report itself. Moreover, the universal availability of Microsoft windows environment and object-oriented feature of this program further its flexibility and widespread application.

SOFTWARE AVAILABILITY

The floppy disc of the software can be obtained from the author by sending a letter of request.

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