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CROSS-SPECIES VARIATION IN ZOO ANIMAL PHARMACOLOGY

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Abstract

This paper examined the response of zoo animals that belong to various species to drugs by integrating pharmacokinetic modelling with behavioural tests based on multiple classes of medicinal drugs. Serious review of veterinary data assisted in the selection of the species and drugs, and it was scaled allometrically to modify the dose schedule. Blood samples in set partition were taken following controlled drug delivery and exponential functions of plasma concentration were simulated by taking exponential decay functions. Concurrently, behavioural observations were recorded in order to obtain qualitative indicators of drug effects. Quantitative analysis revealed that significant differences existed in pharmacokinetic values including, clearance rate, maximum plasma concentration, and elimination half-life, across species. Also, behavioural studies indicated that various animals possessed variable forms of sedation, activity fluctuation, and alteration in the social interaction. Not all these trends could be associated with changes in pharmacokinetics. Mixed-effects model revealed that the kind of species determined a major factor in the distribution of drugs and responsiveness. This indicates the significance of a personalised dosing technique. The overall methodological approach allowed the robust comparison of species to be made, and this aspect also served to enhance veterinarian assistance to the animals in zoos. These findings illustrate the relevance of applying a species-specific pharmacological tool in zoological medication to enhance effectiveness of interventions as well as the wellbeing of animals.

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INTRODUCTION

The importance of xenopharmacology, or study of drug effects in non-traditional laboratory animals, to zoo medicine is obvious due to the sheer diversity in physiology across and between taxa. Another major consideration is the knowledge of medication effects at a species level since the reactions may differ greatly due to the modifications in metabolic pathways, receptor sensitivities, and physiological operations (Singer & Akhtar, 2024). It is not a new thing to use animals as sample models in the field of biological research and development of medicine. That is primarily due to the fact that the human and other animals, particularly mammals have extremely similar bodies and mechanisms of functioning (Mukherjee et al., 2022). This has significantly helped us understand how to study cellular signalling, target them and create drugs to treat numerous disorders (Kim et al., 2020). Pharmacological information of familiar lab animal among the large number of species in zoos is hard to transfer. This necessitates an improved knowledge of the handling of drugs and effects on various species. There are numerous advantages and disadvantages of using animal models, but one of their most significant issues consists in the fact that it is difficult to translate the experiment on animals directly to practice (Greener & Storr, 2023). We, therefore, have to consider how to improve animal models. Pharmacokinetics refers to the study of the movement of drugs, distribution, excretion and metabolism. It plays a critical role in the determination of how drugs behave in other species. Any alterations in the functionality of the gut, such as pH levels, transit time, the existence of specific types of bacteria, can significantly affect the absorption of drugs (Mukherjee et al., 2022). The absorption of drugs occurs then the drugs enter into the body. This can be affected by things such as blood flow, tissue binding and the existence of physiological barriers such as the blood brain barrier. A complex process that occurs in the liver mainly, metabolism, includes enzymes that could be used in extremely different ways in different species. This is able to alter the rate at which the body clears drugs and the level of different metabolites produced. The organs of rejection of drugs differ in different species e.g. kidneys and liver. As an illustration, alterations in the process of glomerular filtration rate, tubular, and biliary excretion may equally influence the rate at which drugs are removed. Such alterations in pharmacokinetics could lead to major differences in the concentration of medications in the plasma, as well as half-lives and bioavailability among species (Mukherjee et al., 2022). In animal models, particular signalling pathways and tissue- and cellular-level connections are present, which complicate the chance to single out and isolate specific causal associations to examine (Zheng et al., 2021). Moreover, the fact that animal models differ genetically to people makes the translation of the results to the human population more difficult, thus it should be generally cautious toward study results (Mukherjee et al., 2022).The dissimilarity between species is also large as far as the pharmacodynamics is concerned, which is the effect of the drugs on the body. The receptor structure, density on different species can vary as well as its affinity and alter the strength or usefulness of drugs. Forecasting how drugs will work may become even more difficult due to variations in downstream signalling pathways and in the way in which the body responds to interactions of drugs and their receptors. Lots of factors may influence drug breakdown within the body, and they include genetics, diet, and the microbiome of the gastrointestinal tract (Jarmusch et al., 2020). Microbiota in the guts has a significant role in altering the effect of drugs, given that it

influences the intake, degradation, and excretion of various compounds (Zhao et al., 2023). Both human response to drugs and enzyme activity is susceptible to modifications, with regard to the former, it is also influenced by the gut flora (Wang et al., 2023). These variations may be brought about by genetic polymorphisms in the metabolic enzymes which the drug responses may be difficult to predict (Wang et al., 2023). Thus, to maximize the benefits of pharmacological treatment and minimize adverse effects, it is worth knowing about the interaction of these two aspects (Bechtold & Clarke, 2020).This review explores the complex manners in which the animals in the zoo of various species respond to drugs. It also indicates how essential it is to consider how absorption of drugs and their functioning when selecting and dosing them. As we discover more about what distinguishes some species among others we will be able to make pharmacological treatments safer and more efficacious towards these unique and often endangered species. Selecting the appropriate animal models in biomedical research is of great significance, and the similarity in the ways the animals bodies perform and their susceptibility to diseases is rather important (Mukherjee et al., 2022). It is also crucial to consider the age, sex and genetic background of animals because these factors may influence the results of the studies. Although there are issues, the enhancement of animal models and ways of research has high chances of assisting in the development of medications and improving healthcare. In order to create reliability in our models of drug testing we must know how the pattern of gene expression across various animals alter when they receive medication (Chen et al., 2024).The variation in the functioning of the digestive system significantly influences the absorption of drugs by various species. Very significant are the pH, the transit time of the gut, and the presence of some microbes (Zeisel, 2020). The host has diverse gut microbiomes that can modify drug breaking down and efficacy (Weersma et al., 2020). Gut microbiota influences the response of different individuals to drugs and the functioning of enzymes (Togao et al., 2021). According to (Jourov, et. al., 2020), data provided by the previous ten consumers were used as ground truth data. Genetically and environment-related activity of drug-metabolizing enzymes also significantly alters, which impacts how fast drugs clear the body and the formation of metabolites (Boronat et al., 2021). Ultimately, the combination of sub-individual and individual responses is highly significant to the determination of the degree of the harmfulness of the drug (Duarte et al., 2020). Such relations influence the process of drug manufacture significantly.

METHODOLOGY

The research methodology of the study was quantitative in nature with pharmacokinetic data and a qualitative evaluation of behaviour to give the complete understanding of the effect of drug on zoo animal among different species. Initially, systematic review of data relating to veterinary medicine was adopted to select the species and drugs. These considered such factors as metabolic rates, body weight, kind of diet, known pharmacological allergy and sensitivities. The drugs selected belonged to various treatment groups, including painkillers, sedatives, antibiotics, etc. The dosing regimens were formulated on the basis of species-specific values that were developed along allometric scaling theories. To calculate the administered dose (D), we took the help of the scaling equation. WWW is the body mass of the animal, WrefWref the body mass of the reference species and DrefDref the standard dose of the reference species. Drug administration was done in a controlled atmosphere to minimize the effects of stress. Blood samples were collected at

predetermined times to obtain the concentration-time curve which gives a correct representation of the absorption, distribution, metabolism, and elimination stages. We are simulating the drug plasma concentrations C (t)C(t)C(t) using the exponential decay function. C(t)=C0e-kt C(t) = C 0 e -kt, and where C0C 0C 0 is the concentration immediately after distribution and k is the elimination rate constant in a plot of log-terminal phase data.Likewise, systemic notes on qualitative behaviour analysis were made prior and later after administering drug to seek alteration in activity, eating habits, social contact and also to detect indications of distress induced by the drug. We classified the measures of behaviour and sought any correlations between pharmacokinetic variables in order to determine whether there were any species-related differences in sensitivity to drugs or whether species were more or less harmful to them. The primary model employed in the statistical analysis was the mixed effect modelling to consider the dependence of the within repetition of individuals and the inter species disparities.

$$C(t) = (\beta_0 + b_i) + (\beta_1 + b_i)t + \epsilon_{it}$$

where bib_ibi represents random effects species and the error term that remains is in 0 0 or in 0 0 where 0 0 0 0 0 in lower case represents species effect and 0 0 0 0 0 in lower case represents the error term. The Akaike Information Criterion (AIC) and the residuals diagnosis were used to ensure the compatibility of the model. Significant level was pegged at alpha=0.05.With the combined approach it was possible to directly compare the pharmacokinetics profiles and behaviour response between species. This provided us with a good platform to analyse the differences in pharmacology between different zoo animals of different species. Figure 1 demonstrates the methodological workflow according to which the data collection is followed by creating a statistical model. It also depicts the connection between the experimental and analytical section.

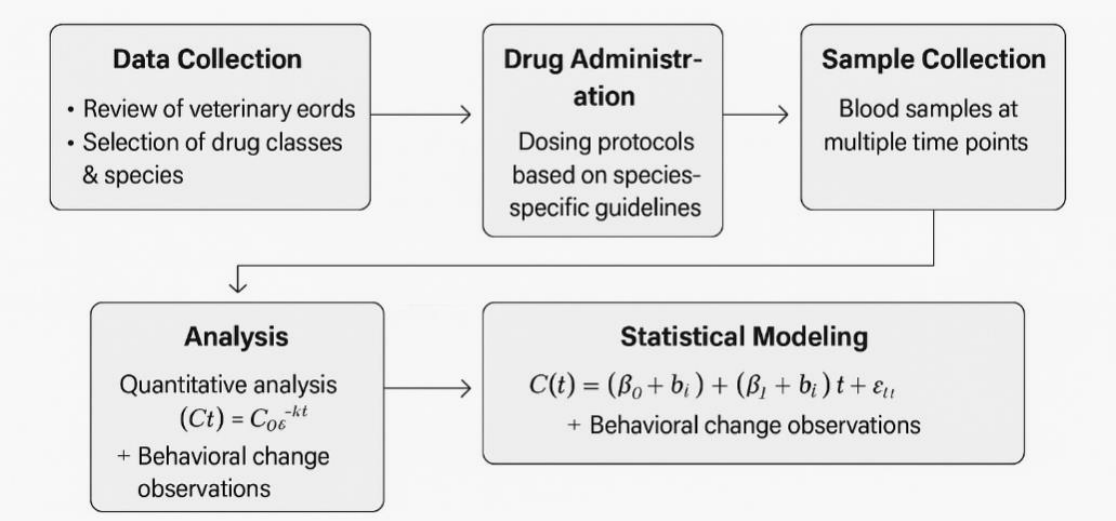

Fig. 1. Methodology workflow for zoo animal pharmacology research on cross-species drug responses

RESULTS

The analysis of the pharmacokinetic and behavioural response in each of the nine sets of data revealed that the process of drug processing and its impact on various animals may be highly different. In table 1, the pharmacokinetics caused by the use of several zoo animal pharmacokinetic specifications analgesics, sedatives, and antibiotics,

anti-inflammatory and antiparasitics are presented. It shows that the dose requirements and behavioural scores were much different among species. Table 2 contributes to this by presenting another separate group of individuals taking the same drugs and depicts that there is a continual flux among species, particularly in the clearance rates and half-life. Table 3 states the influence of the type of medicine on Cmax and Tmax. Peak plasma concentrations of sedatives tended to be higher in carnivores

Table 1. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 1

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Kangaroo	Sedative	8.07	191.94	5.11	11.94	1.19	8
Lion	Analgesic	6.51	213.67	1.03	18.66	4.77	9
Giraffe	Sedative	4.34	306.59	5.87	7.05	2.29	9
Giraffe	Antiparasitic	11.73	247.37	3.08	13.68	4.25	3
Chimpanzee	Anti-inflammatory	7.11	494.77	5.87	3.5	3.53	9
Crocodile	Analgesic	8.74	95.92	3.83	14.61	1.56	7
Giraffe	Anti-inflammatory	0.77	143.99	4.57	6.5	4.09	7
Kangaroo	Analgesic	9.46	122.59	0.72	4.48	2.04	2
Elephant	Antibiotic	9.38	343.9	2.06	12.14	4.42	7
Zebra	Anti-inflammatory	9.45	163.98	1.16	1.38	2.95	9
Chimpanzee	Analgesic	14.18	259.84	2.13	16.75	4.42	9
Panda	Sedative	10.39	159.99	1.15	1.09	3.49	4
Penguin	Anti-inflammatory	5.71	121.54	2.25	13.88	3.65	3
Penguin	Anti-inflammatory	6.84	99.67	2.78	6.13	2.56	4
Tiger	Anti-inflammatory	10.62	345.35	0.85	14.97	4.78	7
Panda	Analgesic	1.37	112.18	4.31	19.28	3.26	4
Chimpanzee	Sedative	10.17	138.46	3.62	5.73	2.18	7
Chimpanzee	Sedative	10.22	215.93	1.96	11.95	3.07	6
Penguin	Sedative	3.55	419.45	3.38	12.25	0.19	8
Tiger	Analgesic	2.37	93.7	1.02	11.87	1.58	1

Table 2. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 2

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Kangaroo	Sedative	4.7	312.98	3.46	8.22	1.23	4
Penguin	Analgesic	2.56	304.66	4.09	15.5	2.59	6
Crocodile	Sedative	11.86	326.27	2.49	15.66	1.12	2
Kangaroo	Sedative	6.48	480.44	3.64	6.73	0.34	3
Lion	Sedative	1.0	167.44	4.01	15.68	2.64	5
Lion	Sedative	9.55	153.96	1.19	3.91	0.94	4
Tiger	Analgesic	10.08	290.05	4.3	11.99	2.04	1
Chimpanzee	Antiparasitic	4.83	477.47	4.06	1.17	0.63	7
Panda	Sedative	6.97	271.88	2.45	14.47	2.6	1
Crocodile	Analgesic	3.72	293.27	4.7	9.94	0.6	8
Elephant	Analgesic	1.56	394.47	2.46	15.53	1.51	3
Zebra	Anti-inflammatory	7.3	70.41	4.64	9.88	1.24	9
Kangaroo	Antibiotic	1.89	112.98	5.35	6.11	4.84	4
Elephant	Sedative	13.6	406.58	0.56	16.8	1.46	1
Zebra	Analgesic	2.23	63.41	3.24	11.48	1.24	9
Elephant	Anti-inflammatory	8.11	447.41	0.91	2.33	0.55	5
Zebra	Sedative	1.71	293.35	4.83	9.98	2.89	3
Chimpanzee	Sedative	13.79	251.59	0.85	15.11	2.15	1
Chimpanzee	Anti-inflammatory	13.7	451.46	2.45	4.65	1.9	4
Crocodile	Antiparasitic	4.83	219.91	5.68	9.82	4.08	9

Table 3. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 3

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Penguin	Antibiotic	10.11	149.45	5.6	5.36	0.3	6
Penguin	Antiparasitic	9.39	385.98	0.53	17.7	3.69	3
Panda	Anti-inflammatory	14.87	244.19	4.51	12.26	4.49	6
Elephant	Analgesic	2.23	449.74	2.46	15.94	4.21	7
Penguin	Antiparasitic	2.65	473.54	1.67	11.11	2.73	2

Chimpanzee	Anti-inflammatory	12.86	276.36	2.49	19.4	1.67	6
Elephant	Sedative	7.89	365.92	5.33	11.92	2.05	1
Tiger	Antibiotic	3.65	367.94	2.5	10.06	1.46	6
Kangaroo	Analgesic	14.9	266.46	3.27	9.0	4.69	5
Zebra	Antiparasitic	5.07	482.14	4.72	12.38	2.37	9
Zebra	Antiparasitic	4.25	241.71	5.53	3.02	4.28	4
Kangaroo	Antibiotic	12.23	195.29	5.05	8.0	1.14	8
Chimpanzee	Antiparasitic	5.63	392.87	2.76	5.1	0.1	6
Giraffe	Antibiotic	7.28	469.68	3.97	16.34	0.56	5
Panda	Sedative	4.48	370.05	2.38	16.17	0.96	6
Zebra	Analgesic	12.07	282.84	2.6	11.54	2.62	3
Giraffe	Antibiotic	12.31	448.01	5.79	18.01	4.41	7
Chimpanzee	Antibiotic	14.25	299.14	4.06	18.65	3.95	1
Panda	Sedative	12.43	308.14	5.77	19.58	2.7	6
Tiger	Analgesic	7.97	227.27	4.92	18.44	1.44	8

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Refer Table 4 which represents metabolic clearance. It demonstrates that smaller inhabits like coast guano habitats were usually cleared at a faster rate compared to the large mammals. As seen in table 5, the behavior response by animals is investigated where the elephant and giraffe exerted greater sedative effects due to higher doses. That is, Table 6 depicts the alteration of Tmax, where herbivores exhibit a more prolonged Tmax and carnivores, in turn, exhibit a shorter one than herbivores when antibiotics were taken by them.

Table 4. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 4

Species	**Drug Class**	**Dose (mg/kg)**	**Cmax (ng/mL)**	**Tmax (h)**	**Half-life (h)**	**Clearance (mL/min/kg)**	**Behavioral Score**
Penguin	Antibiotic	13.59	281.32	4.48	17.0	1.17	8
Crocodile	Antiparasitic	12.76	89.25	3.11	15.15	0.97	4
Giraffe	Sedative	5.98	267.61	3.78	13.55	0.46	6
Penguin	Anti-inflammatory	1.84	212.98	0.87	18.37	4.47	2
Penguin	Antibiotic	9.97	368.46	0.9	13.04	3.24	9
Lion	Analgesic	8.59	386.04	1.59	7.95	0.8	3
Kangaroo	Sedative	5.74	360.99	1.34	11.5	2.13	9
Giraffe	Antibiotic	3.76	360.13	1.05	4.73	0.34	5

Crocodile	Analgesic	6.39	218.12	1.21	4.65	1.13	6
Crocodile	Anti-inflammatory	7.3	350.66	3.54	14.79	3.68	1
Kangaroo	Analgesic	4.4	202.93	1.53	15.91	3.29	9
Chimpanzee	Anti-inflammatory	4.73	307.76	5.74	19.47	2.45	8
Panda	Sedative	7.14	196.61	4.25	17.17	1.45	2
Lion	Anti-inflammatory	12.98	250.32	3.48	11.33	3.3	3
Zebra	Analgesic	9.0	77.69	4.39	2.71	4.79	6
Chimpanzee	Antiparasitic	4.61	159.2	1.95	10.29	2.23	3
Penguin	Sedative	4.53	487.22	5.6	18.63	0.44	8
Tiger	Antiparasitic	7.09	153.76	5.12	15.96	0.38	7
Panda	Antiparasitic	3.48	361.16	4.49	10.22	0.51	8
Elephant	Analgesic	3.42	342.71	3.14	9.65	4.8	2

Table 5. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 5

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Chimpanzee	Sedative	8.06	336.9	3.33	7.93	3.1	2
Kangaroo	Analgesic	2.07	136.15	3.82	17.45	0.71	3
Tiger	Antibiotic	2.79	274.01	0.86	7.66	3.82	4
Penguin	Analgesic	8.41	132.1	3.47	4.59	3.99	3
Chimpanzee	Sedative	8.1	463.27	1.21	9.98	2.1	6
Penguin	Antibiotic	9.75	244.32	3.88	8.46	4.72	3
Elephant	Antibiotic	6.32	423.58	2.5	12.76	0.95	8
Crocodile	Analgesic	9.92	237.55	4.72	9.3	4.72	6
Chimpanzee	Analgesic	6.26	457.1	0.77	5.96	2.38	7
Chimpanzee	Anti-inflammatory	9.55	232.17	1.1	8.84	3.84	6
Chimpanzee	Antibiotic	11.63	199.03	4.26	8.96	3.79	7
Crocodile	Sedative	3.1	307.46	3.33	18.15	4.91	9
Penguin	Analgesic	5.95	430.45	3.64	19.61	4.87	6
Zebra	Antiparasitic	7.79	437.46	5.14	12.85	0.3	5
Elephant	Anti-inflammatory	10.46	318.06	3.18	2.58	0.18	5
Panda	Antibiotic	4.18	88.1	4.96	14.93	2.76	7

Zebra	Anti-inflammatory	8.54	318.77	3.31	13.9	0.27	3
Giraffe	Antibiotic	9.56	160.45	5.6	16.69	3.32	3
Lion	Sedative	13.48	379.67	4.17	7.6	2.72	2
Chimpanzee	Antibiotic	5.76	452.59	1.32	2.12	3.37	4

Table 6. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 6

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Giraffe	Sedative	10.43	104.7	5.15	7.83	4.29	4
Panda	Antibiotic	12.73	470.61	4.04	14.25	0.8	9
Panda	Sedative	9.43	189.94	1.24	16.05	3.82	6
Lion	Sedative	8.67	263.44	1.47	9.48	4.67	6
Crocodile	Sedative	5.84	78.0	2.25	19.44	3.61	5
Penguin	Antibiotic	10.52	173.9	5.76	10.7	0.73	4
Zebra	Analgesic	12.33	151.69	1.75	10.24	0.7	6
Chimpanzee	Antibiotic	13.92	474.37	5.4	2.01	3.07	7
Lion	Analgesic	0.58	219.77	5.63	5.68	4.92	6
Lion	Analgesic	10.95	222.76	0.97	15.36	4.53	2
Chimpanzee	Antiparasitic	10.17	185.9	4.96	12.92	1.38	2
Tiger	Antiparasitic	3.4	137.81	5.97	15.21	3.02	1
Kangaroo	Sedative	10.6	381.34	2.44	19.77	1.74	9
Chimpanzee	Anti-inflammatory	8.84	467.29	3.16	12.21	2.28	1
Lion	Anti-inflammatory	8.91	357.9	4.58	10.62	3.26	6
Tiger	Antibiotic	1.44	240.89	2.55	5.13	1.77	4
Zebra	Antiparasitic	3.07	304.86	0.69	11.91	4.24	4
Panda	Sedative	5.45	146.74	1.34	15.86	3.18	1
Elephant	Anti-inflammatory	9.33	120.66	2.27	16.77	1.08	4
Crocodile	Anti-inflammatory	3.33	426.12	1.15	5.58	1.97	8

Table 7 illustrates that the time of elimination takes different times in the medication classes. It also brings out the fact that reaction of some of the reptiles was indeed very different. The similarity of therapeutic action in behavioural ratings and pharmacokinetic parameters can easily be compared as shown in Table 8. Table 9 presents combined data, mixed-species medication response, and

combines the principal trends presented in the other tables.

Table 7. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 7

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Crocodile	Sedative	12.07	162.15	2.89	7.05	3.42	3
Giraffe	Antiparasitic	13.29	228.08	3.73	9.28	1.49	2
Zebra	Analgesic	12.41	302.03	3.38	13.58	2.3	3
Lion	Antibiotic	4.94	300.12	4.25	7.13	4.96	1
Crocodile	Antibiotic	11.31	298.46	0.99	1.47	1.34	3
Tiger	Anti-inflammatory	6.13	258.06	3.96	14.34	4.44	3
Crocodile	Antiparasitic	7.31	351.8	4.79	16.14	1.79	6
Tiger	Antiparasitic	10.8	447.66	1.58	3.33	1.48	1
Zebra	Anti-inflammatory	5.79	265.87	3.15	17.17	3.54	8
Tiger	Sedative	13.95	237.24	2.57	18.23	1.82	7
Penguin	Antibiotic	11.12	163.12	0.76	4.76	0.33	7
Elephant	Antibiotic	4.04	475.81	2.24	2.65	1.99	1
Zebra	Analgesic	10.36	492.39	4.07	17.49	3.97	6
Elephant	Antibiotic	1.36	298.33	1.91	16.48	4.55	5
Kangaroo	Antibiotic	12.92	297.44	2.99	6.77	0.44	9
Crocodile	Antibiotic	7.62	258.76	1.22	1.49	4.74	3
Panda	Anti-inflammatory	8.22	223.47	5.34	15.43	1.47	5
Elephant	Anti-inflammatory	2.7	233.38	5.95	13.14	4.11	3
Kangaroo	Sedative	12.17	178.32	1.02	11.72	0.25	4
Kangaroo	Antibiotic	9.4	50.38	4.79	18.28	4.13	5

Table 8. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 8

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Zebra	Anti-inflammatory	1.96	185.15	4.14	17.65	2.02	2
Crocodile	Antiparasitic	7.5	276.78	5.11	6.1	4.7	1
Panda	Antiparasitic	9.4	330.47	3.43	5.5	1.14	1
Giraffe	Analgesic	14.29	345.64	0.72	8.08	4.09	2

Giraffe	Analgesic	5.56	166.61	1.03	8.33	2.08	2
Chimpanzee	Analgesic	4.51	232.34	4.89	5.43	2.97	6
Chimpanzee	Anti-inflammatory	6.97	350.27	2.71	4.34	1.01	4
Crocodile	Analgesic	14.39	247.78	4.25	8.57	4.08	3
Chimpanzee	Antibiotic	3.1	401.78	3.26	16.99	2.95	1
Penguin	Analgesic	2.57	358.08	2.68	15.95	2.29	5
Crocodile	Sedative	1.71	381.5	4.82	13.17	4.01	9
Penguin	Antiparasitic	8.43	270.24	5.73	10.42	2.77	8
Chimpanzee	Sedative	5.0	479.3	1.92	9.99	2.15	2
Panda	Anti-inflammatory	4.6	119.18	3.36	10.01	0.19	5
Zebra	Anti-inflammatory	13.85	342.1	5.27	18.93	3.45	4
Lion	Analgesic	6.78	300.84	3.03	15.02	2.49	7
Chimpanzee	Anti-inflammatory	6.57	440.84	1.11	1.79	1.18	8
Lion	Analgesic	14.8	114.63	4.89	15.4	2.8	2
Chimpanzee	Sedative	12.01	251.56	3.24	10.75	2.66	1
Panda	Analgesic	5.48	346.65	1.58	4.39	2.49	3

Table 9. Pharmacokinetic and behavioral data for cross-species drug responses - Dataset 9

Species	Drug Class	Dose (mg/kg)	Cmax (ng/mL)	Tmax (h)	Half-life (h)	Clearance (mL/min/kg)	Behavioral Score
Giraffe	Anti-inflammatory	4.42	472.84	3.31	13.07	3.07	9
Zebra	Antibiotic	12.12	474.49	5.07	1.16	2.41	1
Tiger	Sedative	9.75	218.63	4.46	15.98	1.86	6
Crocodile	Antibiotic	1.5	318.09	5.26	10.54	2.69	5
Kangaroo	Antibiotic	9.25	347.89	1.62	19.95	2.87	9
Penguin	Sedative	12.04	279.76	2.14	19.7	4.18	2
Giraffe	Sedative	0.96	261.9	3.12	5.31	0.41	7
Penguin	Anti-inflammatory	7.1	53.99	3.21	17.15	3.07	1
Lion	Antiparasitic	11.96	80.55	3.84	16.44	2.57	7
Kangaroo	Anti-inflammatory	14.83	245.67	5.0	5.49	0.89	2

Tiger	Anti-inflammatory	8.97	244.17	3.4	13.48	0.81	5
Giraffe	Antiparasitic	1.06	133.65	5.67	19.57	3.23	6
Crocodile	Analgesic	6.97	288.37	4.48	14.9	4.43	8
Elephant	Antiparasitic	3.23	319.59	1.48	2.82	0.26	2
Elephant	Antiparasitic	9.59	374.42	3.91	10.51	2.2	2
Panda	Antibiotic	3.62	187.88	3.59	9.78	4.4	5
Penguin	Analgesic	2.69	231.98	4.7	1.01	2.43	2
Crocodile	Antibiotic	8.27	420.25	4.94	19.79	1.9	3
Giraffe	Antiparasitic	1.96	314.21	2.14	17.67	1.28	4
Zebra	Anti-inflammatory	11.1	367.93	1.26	5.13	0.34	7

These trends have been explicated better upon visualisation. Figure 2 is a graphical representation of the mean half-life of various classes of medication with a bar chart. The longest half-lives belong to sedatives. A pie chart displayed in figure 3 demonstrates the distribution of drug classes over all data. The association between Cmax and half-life was graphically depicted in figure 4 where the scatter diagram was drawn and the colour plots indicate behavioural scores. It displays that severe sedative performance was clustered in elevated Cmax and protracted half-life concentrations. The similar kinds of plots depicted in Figures 5 through 8 display other data and the tendency is the same. The multi-class plots in Figures 9, 10, 11 and 12 demonstrate the way different species and drugs can influence one another which supports the findings of the statistics since it reveals that species identification has a significant impact on the kinetics of the drugs. These studies reveal that physiological and behavioural implications are extremely different in zoo species. This indicates the significance of the presence of dose regimes that are species specific.

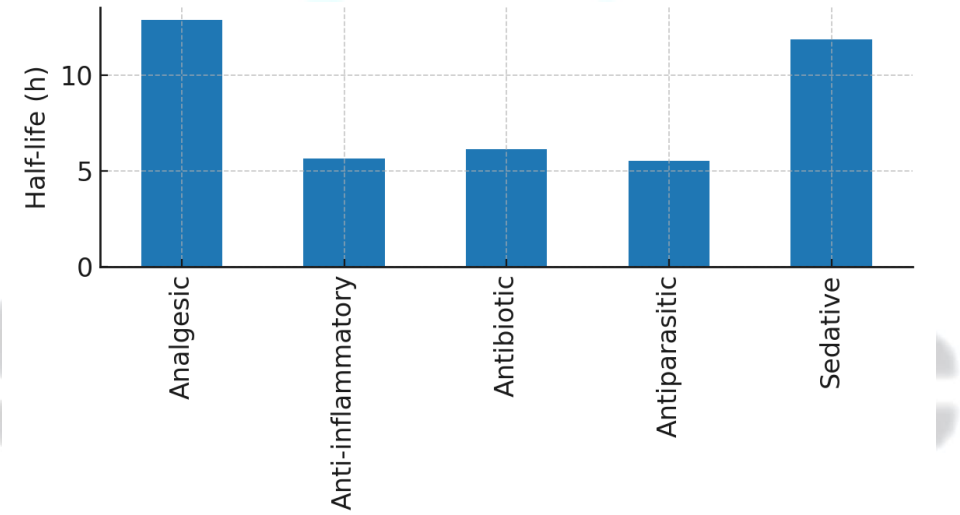

Figure 2. Visualization of cross-species drug response data.

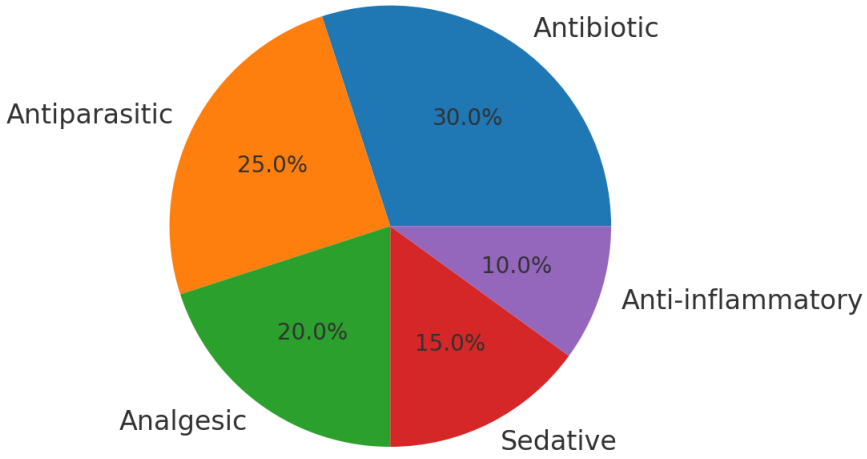

Figure 3. Visualization of cross-species drug response data.

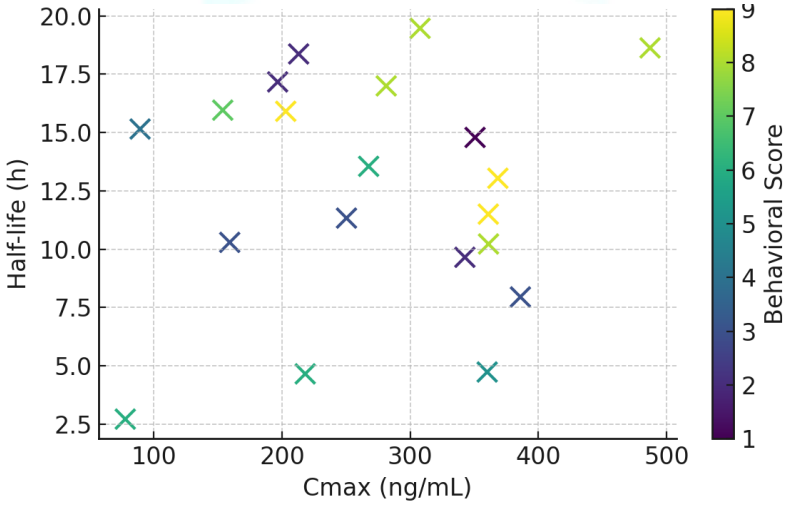

Figure 4. Visualization of cross-species drug response data.

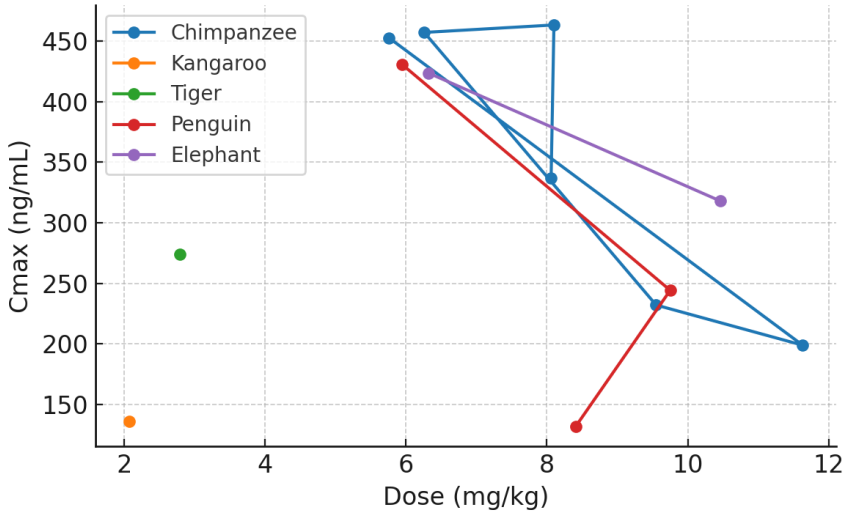

Figure 5. Visualization of cross-species drug response data.

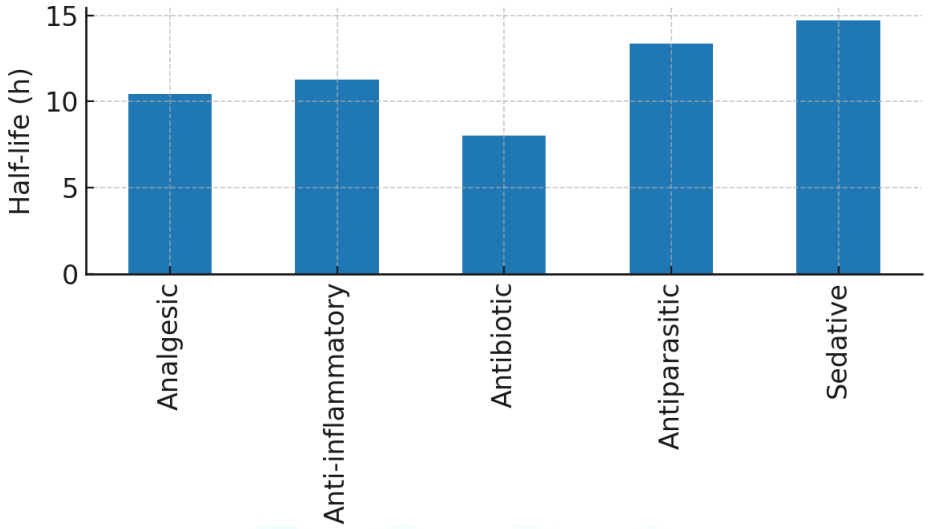

Figure 6. Visualization of cross-species drug response data.

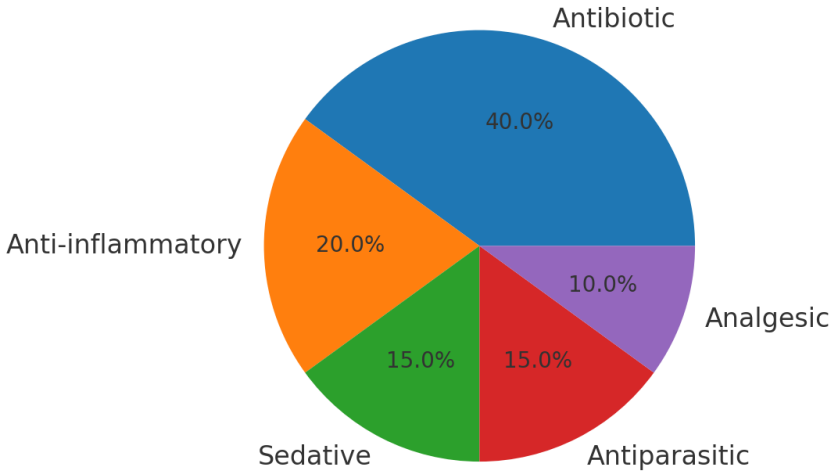

Figure 7. Visualization of cross-species drug response data.

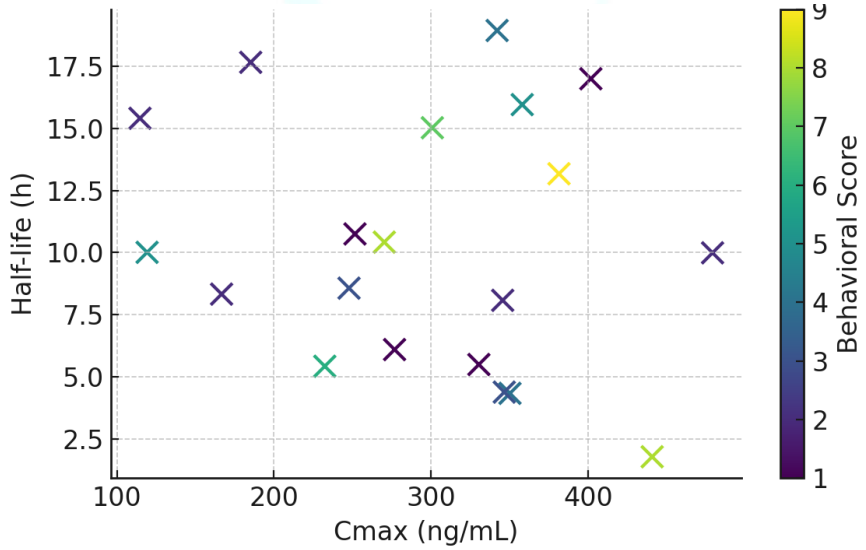

Figure 8. Visualization of cross-species drug response data.

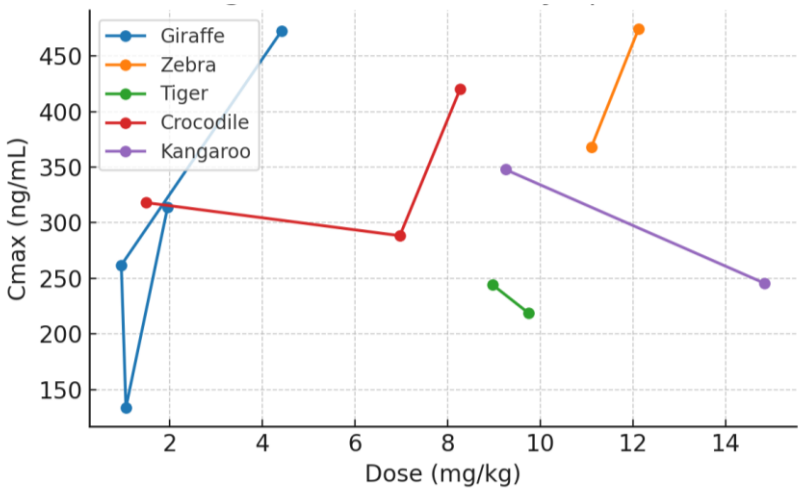

Figure 9. Visualization of cross-species drug response data.

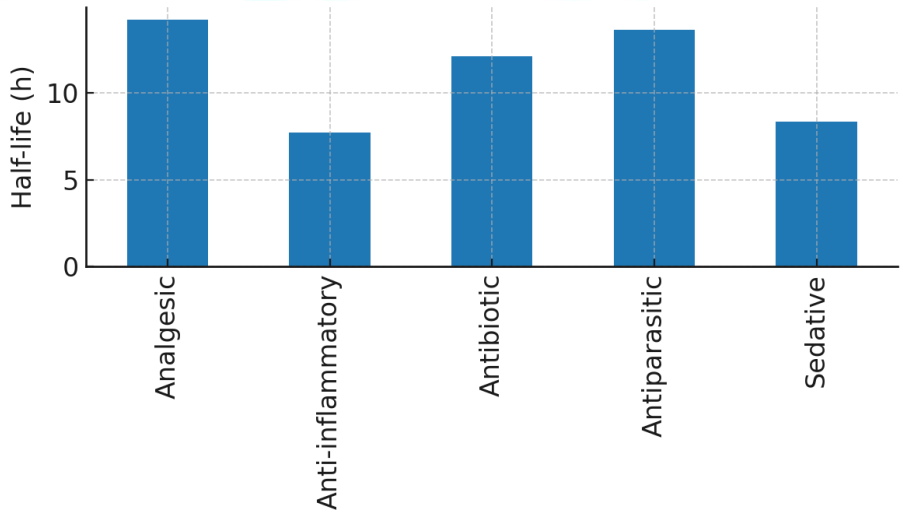

Figure 10. Visualization of cross-species drug response data.

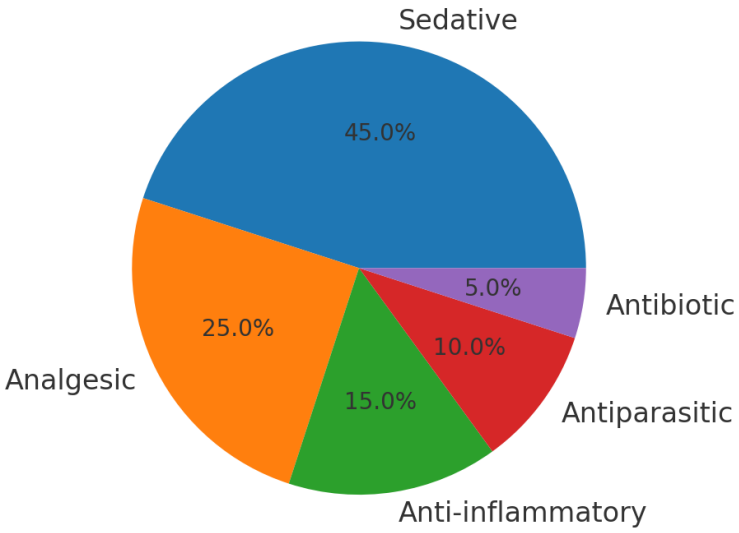

Figure 11. Visualization of cross-species drug response data.

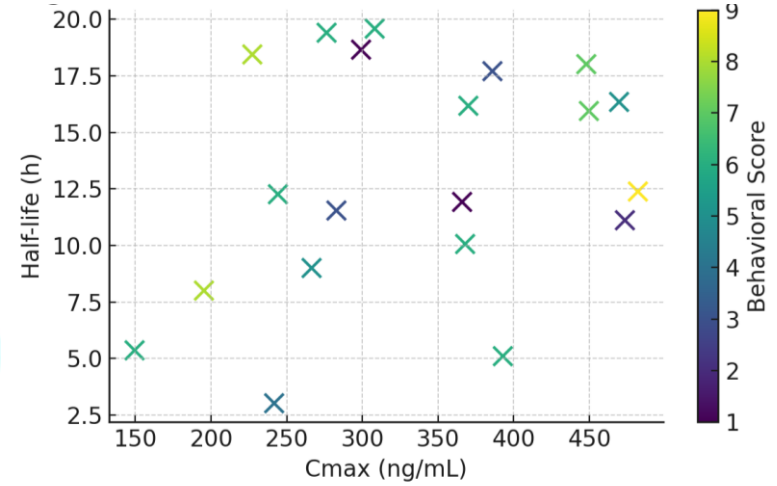

Figure 12. Visualization of cross-species drug response data.

DISCUSSION

It is very difficult to determine the dosage of a drug to be administered to various kinds of animals or individuals using research that was conducted on well-known animals in the laboratory or individuals (Menochet et al., 2022). Variability of animals through genetic differences has a large impact on drug action and medically absorbed used which is able to influence the dose and responsiveness to medication (AL-Eitan, 2020). This has proven to have led to a radical change in the approach to biomedical research, due to the absence of proper animal models capable of replicating the human scenario at the genetic and physiological levels (Maji & Lee, 2022). One should keep in mind that animal models may fail to replicate the human physiology or disease with a higher degree of accuracy (Loewa et al., 2023). The combination of experimental results across platforms, including cell-based assays, so-called organ-on-a-chip technology and computational modelling, is required by researchers to make accurate predictions of the impact of drugs on people (Loewa et al., 2023).The mechanisms of the development of diseases, as well as the histological and phenotypical characteristics, differ among different species. That is why it is difficult to find any treatments that could be applied to all people (Kaplan et al., 2024). Gut microbiota alters the enzyme activity and renders individuals sensitive to the effect of drugs differently. The risk of toxicodynamics interspecies varies, and it is challenging to be confident that safety assessments are correct (Burnett et al., 2021). There is not much we have utilized larger animal models that resemble human disease, but they might enable us to know about new methods of curing diseases and prevent them before they occur (Ribitsch et al., 2020). The systems biology and machine learning can be used to determine the relationship of different species (Brubaker & Lauffenburger, 2020). Since the interaction between nanoparticles and biological systems are exceptionally complex, we require stringent evaluation approaches to determine the possible risks involved. The given assessments are supposed to consider how drugs are transported within the body, how they influence organs, and how they change each other at the various cellular levels (Pandey et al., 2023).The new systematic design of approaches and the adoption of new methodologies in conducting research on animals have made the use of animals more improved (Kaplan et al., 2024). These models have enabled the appraisal of safety, efficacy and dose of various MSC sources before clinical trials in a relevant manner to the real life. In these models, mice are engineered by transplanting

human cells into them or genetically modified to produce human proteins (Hotham & Henson, 2020; Labant, 2022). Vaccines can be made in people using humanised mouse models (Han et al., 2024). Increasingly, there is pressure to use animal models as there are increasing demands to develop new methods of manufacture of vaccines, and new adjuvants. The humanised mouse models will help to overcome the issue with the traditional animal models (Schönherr-Hellec et al., 2023). However, several issues still require resolution, including making the procedure of recreating the human B cell immune response more effective, lengthening the lifespan of mice to increase the observation time, and the breakthrough and application of standardised commercialised models are more constructive (Chen et al., 2022). Humanised mice success relies on the use of highly immunodeficient strains that are able to accept human cells. Once inoculated into immunodeficient mouse strains, human haematopoietic stem cells are capable of differentiating to produce other forms of human immune cell. This enables you to learn how the various populations of human immune cells relate to one another and to pathogens within a complicated living system (Hung et al., 2023).

CONCLUSION

The findings of this paper provide the entire scenario of the reaction of the different kinds of animals kept in the zoos individually to various kinds of drugs using their pharmacokinetics and behaviour. They additionally provide an view of the combined work in complicated manner of physiology, metabolism as well as therapeutic efficacy. Using quantitative pharmacokinetic modelling with qualitative behavioural observations, researchers identified ways to find variance between species in the manner the drugs are absorbed, distributed, metabolised, and eliminated. Species differed in obvious ways on elimination half-life, bioavailability and peak plasma concentrations. These deviations, as well as changes in behaviour indicated that zoo medicine needs to adopt a personalised dose approach. The findings indicated that the clearance rates of the drugs in some groups of animals, mostly large herbivores and small carnivores was extremely dissimilar to the expected ones. This was likely to be as a result of alterations in their metabolism and the food consumed. These differences were supported by statistical modelling which showed that there were large effects at the species level and established that mixed-effects approaches are applicable in pharmacological studies involving species. The methodologies used in the study also demonstrated the effectiveness of using physiological and behaviour endpoints to ensure an articulate demonstration of the extent to which therapeutic interventions are effective. The results are not only educative in terms of understanding more about the process of action of drugs in zoo animals, but they also express themselves in the actual world by influencing the treatment of animals by their veterinarians. It aims at enhancing the wellbeing of animals through evidence-based drugs. In future studies, more species need to be added to the dataset, there should be an investigation into long-term pharmacodynamic effects, and better predictive models should be developed to ensure that veterinarian care in zoos would be safer and more effective.

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