

**THE PARADOX OF HUMAN  
EQUIVALENT DOSE FORMULA – A  
CANONICAL CASE STUDY OF  
PIROXICAM (FELDENE) IN  
MONOGASTRIC ANIMALS**

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**PIROXICAM IS A NON-STEROIDAL ANTI-INFLAMMATORY ANALGESIC THAT CAN CAUSE ALCKERATION OF MUCOSAL LINING AND BLEEDING OF GASTROINTESTINAL TRACT. IT IS ALSO TOXIC TO KIDNEY. THE DAILY DOSE FOR AVERAGE ADULT HUMAN IS 10-40 MILLIGRAMMES**

**ALLOMETRIC SCALING IS AN EMPIRICAL EXAMINATION OF THE RELATIONSHIP BETWEEN THE PHARMACOKINETIC PARAMETERS AND SIZE (USUALLY BODY WEIGHT, RATIO OF ORGAN & BODY WEIGHT, BREATHING NUMBER ETC). THE ALLOMETRIC EQUATION IS:**

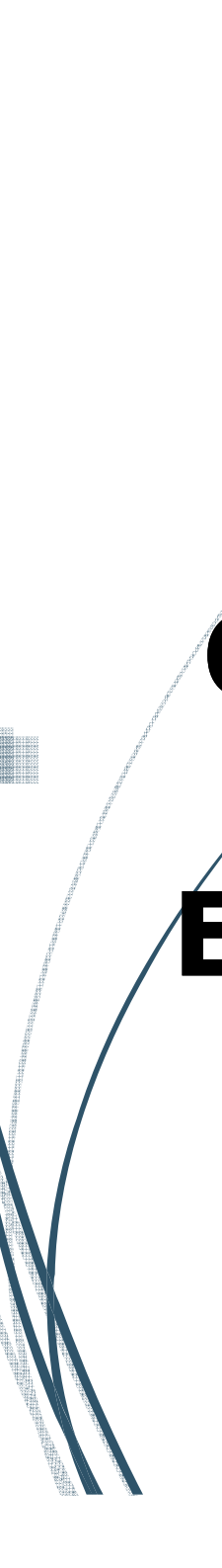
$$\frac{P}{BW} = a(BW)^m$$

**WHERE P = PHYSIOLOGICAL PROPERTY OR ANATOMIC SIZE**

**a = EMPIRICAL COEFFICIENT**

**BW = BODYWEIGHT**

**m = ALLOMETRIC EXPONENT**



**THE SURFACE AREA STILL FINDS  
WIDE ACCEPTANCE IN THE  
CLINICAL LITERATURE, AND IS AT  
NO MORE THAN A ROUGH  
EMPIRICAL APPROXIMATION EVEN  
FOR HOMOIOTHERMS.**

**BODY SURFACE AREA (BSA) IS  
EQUAL TO: BODY WEIGHT (kg)<sup>2/3</sup> x  
10<sup>-4</sup> x K**

**K FOR DOG = 10.1**

**K FOR CAT = 10.0**

**EMPIRICAL COEFFICIENT = 10<sup>-4</sup>  
THE BODY WEIGHT EXPONENTS <sup>2/3</sup>  
OR <sup>3/4</sup> CAN BE USED**



**BUT  $\frac{3}{4}$  EXPONENT GIVES A HIGHER  
DOSE THAN  $\frac{2}{3}$ , HENCE SHOULD  
NOT BE APPLIED**



**DOG\*, CAT, MONKEY\*, BABOON\*,  
RABBIT\*, MICRO-PIG, MINI-PIG,  
SQUIRREL MONKEY, MARMOSET,  
FERRET, GUINEA – PIG\*,  
HARMSTER, RAT & MOUSE**

**HUMAN EQUIVALENT DOSE (HED) WHICH IS  
EQUAL TO ANIMAL DOSE (AD) MULTIPLIED  
BY ANIMAL KM DIVIDED BY HUMAN KM WAS  
USED TO PROJECT THE THERAPEUTIC DOSE  
OF PIROXICAM IN SEVEN (7) MONOGASTRIC  
ANIMALS.**

$$\text{HED} = \frac{AD \times AK_m}{HK_m}$$

**WHEREAS KM FACTOR IS BODY WEIGHT  
(KG) DIVIDED BY BODY SURFACE AREA (m<sup>2</sup>)**

$$K_m = \frac{BW}{BSA}$$



**HUMAN EQUIVALENT NO-OBSERVABLE ADVERSE EFFECT DOSES WHERE DETERMINED BY MULTIPLYING ANIMAL NO-OBSERVABLE ADVERSE EFFECT DOSE BY ANIMAL WEIGHT (AW) DIVIDED BY HUMAN WEIGHT (HW).**

$$\mathbf{HENAED} = \frac{\mathbf{ANAED} \times \mathbf{A_w}}{\mathbf{H_w}}$$

**TABLE: HUMAN-MONOGASTRIC ANIMAL EQUIVALENCE DOSES OF PIROXICAM (20 MILLIGRAMMES)**

| S/No | Species         | Body weight (kg) | BSA (m <sup>2</sup> ) | K <sub>m</sub> Factor | Therapeutic Dose (mg) | Total Translated Dose (mg) | Total given in Literature (mg) |
|------|-----------------|------------------|-----------------------|-----------------------|-----------------------|----------------------------|--------------------------------|
| 1.   | Mouse           | 0.02             | 0.007                 | 2.9                   | 3.6                   | 0.072*                     |                                |
| 2.   | Hamster         | 0.08             | 0.02                  | 4.0                   | 2.6                   | 0.2*                       |                                |
| 3.   | Rat             | 0.15             | 0.025                 | 6.0                   | 1.7                   | 0.25*                      |                                |
| 4.   | Guinea pig      | 0.4              | 0.069                 | 5.8                   | 1.8                   | 0.72*                      |                                |
| 5.   | Rabbit          | 1.8              | 0.15                  | 12.0                  | 0.89                  | 1.6                        | -                              |
| 6.   | Monkey          | 3.0              | 0.24                  | 12.5                  | 0.85                  | 2.5                        | -                              |
| 7.   | Baboon          | 12               | 0.6                   | 20.0                  | 0.53                  | 6.3                        | -                              |
| 8.   | Ferret          | 0.3              | 0.043                 | 7.0                   | 1.53                  | 0.45*                      |                                |
| 9.   | Marmoset        | 0.35             | 0.06                  | 5.8                   | 1.84                  | 0.64*                      |                                |
| 10.  | Squirrel monkey | 0.6              | 0.09                  | 6.7                   | 1.59                  | 0.95*                      |                                |
| 11.  | Cat             | 7.0              | 0.37                  | 18.9                  | 0.56                  | 3.9*                       | -                              |
| 12.  | Dog*            | 10               | 0.5                   | 20.0                  | 0.53*                 | 5.3*                       | 3 – 5                          |
| 13.  | Micro-pig       | 20               | 0.74                  | 27.0                  | 0.39                  | 7.8                        | -                              |
| 14.  | Mini-pig        | 40               | 1.14                  | 35.1                  | 0.30*                 | 12**                       | -                              |
| 15.  | Adult human     | 70               | 1.86                  | 37.6                  | 0.285                 | -                          | 10-40**                        |

**\*SINGLE DOSES OF PIROXICAM (20 - 40 MG) IN HUMAN ARE REASONABLY EFFECTIVE FOR TREATING MODERATE TO SEVERE POST-OPERATIVE PAINS AND COMPARE FAVOURABLY WITH OPIOID ANALGESICS SUCH AS DEXTROPROPOXYPHENE AND TRAMADOL**

**\*FEW ADVERSE EFFECTS WERE REPORTED AND PIROXICAM APPEARS TO BE FAIRLY TOLERATED IN THIS CLINICAL CONTEXT**

**\*IN MULTIPLE DOSING THE ADVERSE EFFECT PROFILE MAY BE MORE PROMINENT, THEREFORE, THERE IS A DEFINITE NEED TO BE ABLE TO QUANTITATIVELY ASSESS THE EFFICACY AND ADVERSE EFFECTS OF PIROXICAM IN PROLONGED DOSING REGIMENS (MOORE ET AL., 2010).**

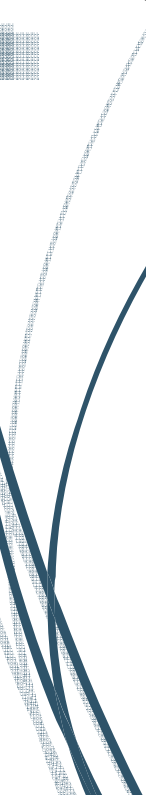
**THE EXTRAPOLATED HIGH DOSES OF  
PIROXICAM FOR MONOGASTRIC  
ANIMALS AGREES WITH THE REPORTS OF  
CALEJESAN ET AL. (2000),  
SUKUMARANNAR ET AL. (2002) AND  
HELLYER ET AL. (2007) INDICATING  
THAT ANIMALS FEEL MORE PAIN THAN  
HUMANS, SINCE THEY POSSESS MORE  
DIFFUSE NEURAL NETWORKS.**

**THE EXTRAPOLATED DOSE OF  
PIROXICAM (1.7 MG/KG) AGREES  
WITH THE REPORT OF UDEGBUNAM ET  
AL. (2012) INDICATING THAT  
PIROXICAM (5MG/GK) ALLEVIATED  
PAIN AND STRESS ASSOCIATED WITH  
WOUNDS IN RATS WITH MINIMAL  
SIDE EFFECTS.**

**STURMAN AND SMITH (1967)  
REPORTED THAT RHESUS MONKEY,  
RABBIT AND GUINEA-PIG RESEMBLE  
MAN IN HAVING A RELATIVELY HIGH  
AFFINITY FOR BINDING SALICYTE A  
NSAIDS SIMILAR TO PIROXICAM IN  
PHARMACOLOGICAL ACTION. BUT  
BABOON, DOG, RAT AND MOUSE HAD A  
LOW BINDING CAPACITY.**

**GASTRIC LESION AND RENAL PAPILLAR NECROSIS HAVE OCCURRED IN DOGS RECEIVING 1 MG/KG DAILY (GALBRAITH AND MCKELLAR, 1991; KNAPP ET AL., 1992). HOWEVER, LITTLE EVIDENCE OF TOXICITY (GASTROINTESTINAL BLEEDING) WAS NOTED AFTER ADMINISTRATION OF 0.3 MG/KG EVERY OTHER DAY (GALBRAITH AND MCKELLAR, 1991; KNAPP ET AL., 1992).**





**EXTRAPOLATION FROM USE IN HUMANS TO DOGS SHOULD BE DONE CAUTIOUSLY BECAUSE OF POSSIBLE DIFFERENCES IN VOLUME OF DISTRIBUTION, THERAPEUTIC CONCENTRATIONS OR SAFETY MARGIN (BOOTHE, 2001).**

## **CONCLUSION:**

- i. THE EXTRAPOLATED TOTAL DOSES FOR DOG (10kg), CAT (7kg), RABBIT (1.8kg), MONKEY (3kg), BABOON (6.3kg), MICRO-PIG (20kg) AND MINI-PIG (40kg) ARE 5.3, 3.9, 1.6, 2.5, 6.3, 1.6mg RESPECTIVELY**
- ii. LITERATURE SEARCH HAS SHOWN A TOTAL OF 3-5mg FOR DOG WEIGHING 10kg**
- iii. FOR A DOG WEIGHING 10kg, A DOSE OF 5.3 MILLIGRAMM SHOULD NOT BE EXCEEDED, AND THE SAME PRINCIPLE APPLIES TO THE REST OF EXTRAPOLATED DOSES, SINCE THE DOSES HAVE NOT BEEN EVALUATED**
- iv. LABORATORY TEST CAN BE CARRIED OUT FOR VALIDATION OF THE EXTRAPOLATED DOSES.**
- v. THE ROUGH ESTIMATION OF THERAPEUTIC DOSES FOR HUMAN DRUGS WHOSE ANIMAL DOSES HAVE NOT BEEN DETERMINED IS EVIDENT IN VETERINARY CLINICAL PRACTICE.**

## **REFERENCES:**

**BOOTHE, 2001 CALEJESAN ET AL., 2000**

**DUBOIS & DUBOIS, 1915, 1916**

**GALBRATH AND MCKELLAR, 1991**

**HELLYER ET AL. 2007**

**MOORE ET AL., 2010**

**PLUNKETT, 2001, KAPP ET AL., 1992, 1994**

## **REFERENCES:**

**REAGAN-SHAW ET AL., 2007**

**SAGANUWAN, 2012**

**SAGANUWAN & ONYEYILI, 2014**


**STURMAN AND SMITH, 1967**

**SUKUMARANNAR ET AL., 2002**

**UDEGBUNA, ET AL., 2012**

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CLIENTS AND PATIENTS**





**THANKS FOR  
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