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Determination of Dermal Penetration Efficiency of [^{14}C] Fenbutatin Oxide in Wistar Rats

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ABSTRACT

This study was conducted following guidelines of US EPA OPPTS 870.7600 to evaluate the extent of penetration of Fenbutatin oxide (FBTO) into the skin of Wistar rats at different time points post dosing. A pilot study was conducted at single dose of 2 mg/cm^2 of FBTO prepared in corn oil with ≈10 μCi of the radioactivity which was applied on the skin of 2 male rats. The site of application was covered using specially designed 'O' ring to avoid the direct contact of test item with adhesive tape. The total recovered radioactivity through exhaled air in first 24 h of pilot study was <1% of total applied radioactivity. So, main study was conducted without exhaled air collection. A single dose of 0.02 (phase 1), 0.2 (phase 2) and 2.0 (phase 3) mg of FBTO /cm^2 of skin with ≈ 10 μCi of the radioactivity was applied to 24 male rats per dose level. Urine, faces, cage wash, cotton swab, 'O' ring, applicator, whole blood, exposed skin, brain, muscle, heart, kidney, lung, liver and residual carcass were collected at 0.5, 1, 2, 4, 10 and 24 h post dosing. A fix quantity of each sample was weighed, processed and analyzed for radioactivity using liquid scintillation analyzer. Percent absorbed, absorbable and dose of test item not absorbed through skin was determined.

The mean dose absorbed at all three dose levels through skin was around 1.837 ± 0.846 %. The mean dose which could get absorbed through skin, if dermal exposure increased (absorbable dose) was 13.18 ± 1.18 % whereas approximately 84.98% dose of FBOT remained unabsorbed on the rat skin. Based on the results obtained in this study, it was concluded that maximum quantity of FBOT was remained unabsorbed during 24 hours of dermal exposure. However, dermal penetration of FBTO was increased in time dependant manner from 0.5 to 24 hours after dermal application which may be continued with increased time of exposure considering the absorbable dose level in skin.

INTRODUCTION TO STUDY PROCEDURE

Test Item	Fenbutatin Oxide Technical (FBTO)
Test System & Groups	Male Wistar rats Hsd:ICR (CD-1®) 2 rats for pilot phase. 24 rats for each phase, total three phase
Guideline	EPA OPPTS 870.7600
Duration of treatment	Single dose application dermally
Dose Levels	Pilot phase: 2.0 mg/cm2 along with ≈ 10 μCi radioactivity (14C), Phase 1: 0.02 mg/cm2 along with ≈ 10 μCi radioactivity (14C). Phase 2: 0.2 mg/cm2 along with ≈ 10 μCi radioactivity (14C), Phase 3: 2.0 mg/cm2 along with ≈ 10 μCi radioactivity (14C)

RESULTS

Table 1: Mean Values of Different Parameters of Phase 1 Study

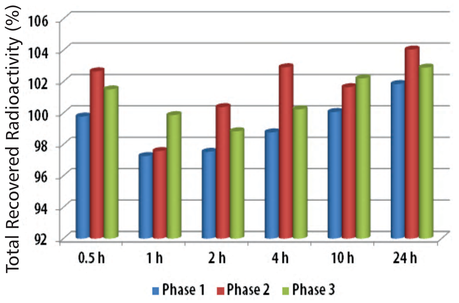
Time (Hour)	Actual Applied ^{14}C FBT (μCi)	Dosing Efficiency (%)	Dose not Absorbed		Absorbable Dose (Dose in washed Skin)		Absorbed Dose	
			μCi	%	μCi	%	μCi	%
0.5	9.67	90.71	9.47	97.93	0.094	0.98	0.070	0.73
1	9.80	91.95	9.31	95.07	0.13	1.29	0.075	0.76
2	9.74	91.43	9.28	95.21	0.13	1.52	0.064	0.66
4	9.72	91.22	9.31	95.83	0.21	2.20	0.059	0.61
10	9.53	89.48	8.75	91.76	0.66	6.91	0.099	1.04
24	9.77	91.67	8.47	86.71	1.15	11.82	0.28	2.81

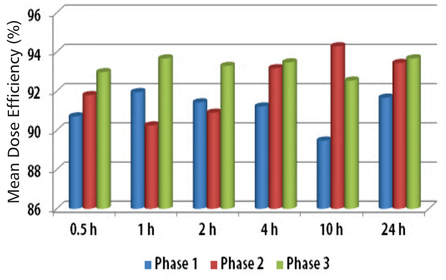
Table 2: Mean Values of Different Parameters of Phase 2 Study

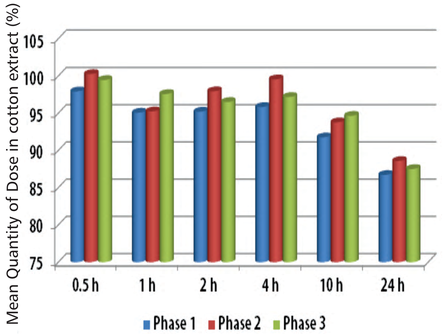
Time (Hour)	Actual Applied ^{14}C FBT (μCi)	Dosing Efficiency (%)	Dose not Absorbed		Absorbable Dose (Dose in washed Skin)		Absorbed Dose	
			μCi	%	μCi	%	μCi	%
0.5	9.34	91.80	9.36	100.26	0.13	1.40	0.094	1.01
1	9.18	90.25	8.74	95.25	0.13	1.43	0.073	0.79
2	9.25	90.90	9.07	97.95	0.16	1.74	0.058	0.63
4	9.48	93.17	9.44	99.55	0.24	2.54	0.058	0.61
10	9.59	94.29	8.99	93.78	0.67	6.94	0.061	0.63
24	9.51	93.44	8.42	88.59	1.32	13.88	0.14	1.42

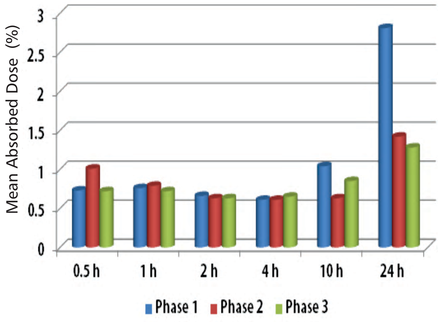
Table 3: Mean Values of Different Parameters of Phase 3 Study

Time (Hour)	Actual Applied ^{14}C FBT (μCi)	Dosing Efficiency (%)	Dose not Absorbed		Absorbable Dose (Dose in washed Skin)		Absorbed Dose	
			μCi	%	μCi	%	μCi	%
0.5	9.52	92.97	9.46	99.46	0.12	1.31	0.068	0.72
1	9.59	93.67	9.36	97.57	0.13	1.38	0.069	0.72
2	9.55	93.29	9.21	96.51	0.15	1.57	0.060	0.63
4	9.57	93.47	9.30	97.18	0.23	2.37	0.062	0.65
10	9.47	92.54	8.96	94.65	0.63	6.66	0.081	0.85
24	9.59	93.67	8.39	87.51	1.33	13.84	0.12	1.28









CONCLUSION

Based on result of this study, it was observed that the maximum percent absorbed dose of Fenbutatin oxide was 2.81, 1.42 and 1.28 and percent absorbable dose was 11.82, 13.88 and 13.84 when applied on skin for maximum time period of 24 hours at dose level of 0.02, 0.2 and 2.0 mg/cm2 (non-radiolabelled along with ≈ 10μCi of the radioactivity), respectively. It could be concluded that the dermal penetration of Fenbutatin oxide was increased in time dependant manner till 24 h after dermal application in male Wistar rats which may be continue with increased time of exposure considering the absorbable dose level in skin under the procedure and conditions followed in the present study.