CHAPTER - IX

PHARMACODYNAMIC EVALUATION OF MUCOADHESIVE MICROSPHERES AND CYCLODEXTRIN COMPLEXES OF ACECLOFENAC

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Evaluation of Anti inflammatory activity

The anti inflammatory activity of aceclofenac and its mucoadhesive microspheres and cyclodextrin complexes was evaluated by carrageenan induced paw oedema model employing zeitlin's apparatus to measure the paw thickness. The products were tested at a dose equivalent to 10 mg/kg of aceclofenac. Sprague dolly rats of male sex weighing between 250 – 300 g were used. The animals were fasted overnight and allowed water ad libitum. The animals were divided into groups of six each. The following are the treatments allotted to each group.

Group 1 – 0.5 ml of 1 % sodium CMC mucilage (control)

Group 2 – Aceclofenac in 0.5 ml of 1 % sodium CMC mucilage

Group 3 – HPMC microspheres of aceclofenac in 0.5 ml of 1 % sodium CMC mucilage

Group 4 – Carbopol microspheres of aceclofenac in 0.5 ml of 1 % sodium CMC mucilage

Group 5 – Aceclofenac - β CD (1:3) complex in 0.5 ml of 1 % sodium CMC mucilage

Group 6 – Aceclofenac- HP β CD (1:3) complex in 0.5 ml of 1 % sodium CMC mucilage

One hour after oral treatment with test preparation (treatment), 0.1 ml of carrageenan suspension (1 %) was injected subcutaneously into the subplantar tissue of the right hind foot and 0.1 ml of saline was injected into the subplantar tissue of the left hind foot. The paw thickness was determined at 0, 0.5, 1, 2, 3 and 4 hours after administration of carrageeenan. The percentage increase in paw thickness and percent inhibition of paw oedema thickness (i.e. anti inflammatory activity) were calculated from paw thickness measurements as follows:

$$\text{Percentage increase in paw thickness} = \frac{Y_t - Y_o}{Y_o} \times 100$$

Y_t = Paw thickness at the time 't' hours (after injection)

Y_o = Paw thickness at the time '0' hours (before injection)

$$\text{Percentage inhibition} = 100 \left[1 - \frac{Y_t}{Y_c} \right]$$

Y_t = Average increase in paw thickness in groups treated with test preparations

Y_c = Average increase in paw thickness in control group

The results are given in Tables 9.1 – 9.6

Table 9.1 Anti – inflammatory Activity of Aceclofenac

Time (h)	Paw Thickness measurement		Percentage increase in paw Thickness		Percentage Inhibition
	Carrageenan	Drug Treated	Carrageenan	Drug treated	
0	33.8 ± 1.2	36.0 ± 1.4	0	0	0
0.5	42.4 ± 0.6	37.4 ± 1.0	25.44	3.88	84.74
1	47.4 ± 0.8	39.0 ± 1.2	40.23	8.33	79.29
2	52.1 ± 2.0	40.4 ± 0.6	54.14	12.22	77.42
3	51.0 ± 2.1	40.6 ± 0.8	50.88	12.77	74.9
4	49.8 ± 1.6	40.2 ± 2.0	47.33	11.66	75.3

Table 9.2

Anti – inflammatory Activity of HPMC Microspheres of Aceclofenac

Time (h)	Paw Thickness measurement		Percentage increase in paw Thickness		Percentage Inhibition
	Carrageenan	Drug Treated	Carrageenan	Drug treated	
0	33.8 ± 1.2	37.7 ± 1.6	0	0	-
0.5	42.4 ± 0.6	37.9 ± 1.8	25.44	0.53	97.9
1	47.4 ± 0.8	38.0 ± 2.0	40.23	0.79	98.03
2	52.1 ± 2.0	38.6 ± 2.1	54.14	2.38	95.60
3	51.0 ± 2.1	39.3 ± 0.6	50.88	4.24	91.66
4	49.8 ± 1.6	38.7 ± 0.9	47.33	2.65	94.40

Table 9.3

Anti – inflammatory Activity of Carbopol Microspheres of Aceclofenac

Time (h)	Paw Thickness measurement		Percentage increase in paw Thickness		Percentage Inhibition
	Carrageenan	Drug Treated	Carrageenan	Drug treated	
0	33.8 ± 1.2	36.4 ± 1.2	0	0	-
0.5	42.4 ± 0.6	36.7 ± 1.4	25.44	0.824	96.76
1	47.4 ± 0.8	36.3 ± 0.8	40.23	-0.274	100.6
2	52.1 ± 2.0	36.7 ± 0.9	54.14	0.824	98.47
3	51.0 ± 2.1	37.0 ± 1.2	50.88	1.648	96.76
4	49.8 ± 1.6	37.2 ± 1.4	47.33	2.197	95.35

Table 9.4 Anti – inflammatory Activity of of Aceclofenac – β CD Complex

Time (h)	Paw Thickness measurement		Percentage increase in paw Thickness		Percentage Inhibition
	Carrageenan	Drug Treated	Carrageenan	Drug treated	
0	33.8 ± 1.2	36.6 ± 0.6	0	0	-
0.5	42.4 ± 0.6	36.7 ± 0.8	25.44	.273	98.92
1	47.4 ± 0.8	36.5 ±1.2	40.23	-0.273	100.67
2	52.1 ± 2.0	36.7 ± 1.4	54.14	0.273	99.49
3	51.0 ± 2.1	37.1 ± 1.4	50.88	1.36	97.31
4	49.8 ± 1.6	37.4 ± 2.0	47.33	2.185	95.38

Table 9.5 Anti – inflammatory Activity of Aceclofenac – HP β CD Complex

Time (h)	Paw Thickness measurement		Percentage increase in paw Thickness		Percentage Inhibition
	Carrageenan	Drug Treated	Carrageenan	Drug treated	
0	33.8 ± 1.2	36.4 ± 1.2	0	0	-
0.5	42.4 ± 0.6	36.5 ± 1.8	25.44	0.274	98.92
1	47.4 ± 0.8	36.5 ± 1.6	40.23	0.274	99.31
2	52.1 ± 2.0	36.7 ± 2.0	54.14	0.824	98.47
3	51.0 ± 2.1	37.2 ± 2.1	50.88	2.197	95.68
4	49.8 ± 1.6	37.3 ± 1.4	47.33	2.47	94.78

Table 9.6

Anti- inflammatory activity of Aceclofenac and its Mucoadhesive Microspheres and CD Complexes

Product	Percentage Decrease in Paw Thickness at Time (h)				
	0.5	**1.0**	**2.0**	**3.0**	**4.0**
Aceclofenac	84.74	79.29	77.42	74.9	75.3
HPMC Microspheres	97.90	98.03	95.60	91.66	94.40
Carbopol Microspheres	96.76	100.6	98.47	96.76	95.35
Aceclofenac – β CD	98.92	100.67	99.49	97.31	95.38
Aceclofenac – HP β CD	98.92	99.31	98.47	95.68	94.79

RESULTS AND DISCUSSION

Percentage increase in paw thickness (inflammation) and percentage inhibition of inflammation in control group and groups treated with aceclofenac products are given in Tables 9.1 – 9.6.

In control group which received carrageenan alone, a rapid increase in paw thickness (i.e. inflammation) was observed and a maximum increase of 54.14 % was observed at 2 h after administration and the inflammation was sustained during the period of study.

In the groups which received aceclofenac and its mucoadhesive microspheres and CD complexes (test Products), the percentage increase in paw thickness was low when compared to the control group indicating that all the test products posses good anti-inflammatory activity. The inflammation due to carrageenan was markedly inhibited by the test products. The percentage inhibition was much higher in the initial time points with aceclofenac mucoadhesive microspheres and CD complexes when compared to that of aceclofenac pure drug. A comparison of the percentage inhibition of inflammation (i.e. anti – inflammatory activity) of various products is made in Table 9.6.

The inflammation due to carrageenan was reduced rapidly and to a greater extent in the case of aceclofenac mucoadhesive microspheres and CD complexes when compared to aceclofenac pure drug.

These results indicated the rapid onset of action and higher activity during the initial periods after administration in the case of aceclofenac mucoadhesive microspheres and CD complexes due to their enhanced dissolution and absorption rates.