

The GABA B Receptor Agonist Baclofen Attenuates Chronic Pain in Mice

Bambang Subakti Zulkarnain
Nofitri Wulandari
Junaidi Khotib

Department of Clinical Pharmacy
Faculty of Pharmacy – Airlangga University
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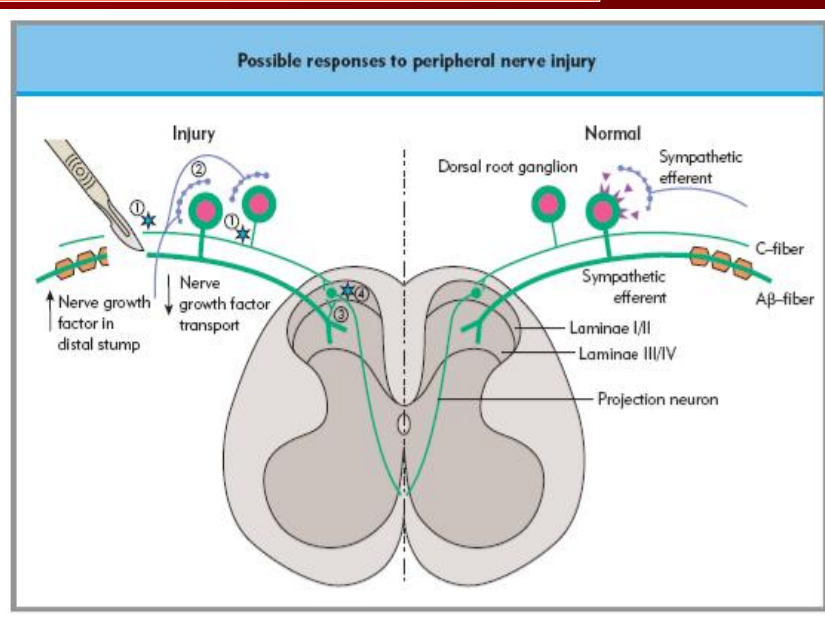
Introduction

- Pain – unpleasant sensoric and emotional experience due to actual or potential tissue damage
- Pain – Acute & Chronic
- Acute Pain – normal physiologic response to dangerous stimuli, limited with time
- Chronic Pain – Persistent process, sustained after the cause has been diminished (Inflammatory & Neuropathic)

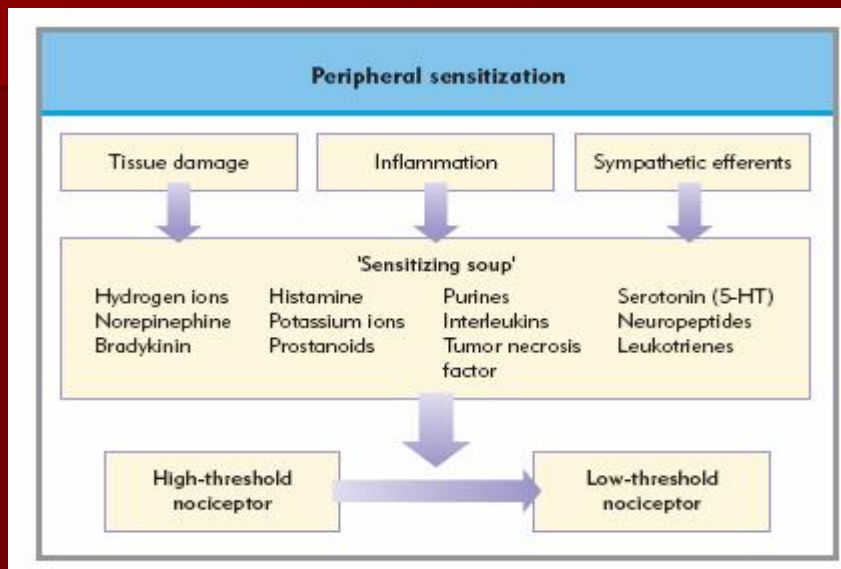
Introduction

- > 90% disease is associated with pain → 40% develop into chronic pain
- Prevalence ↑ → aging population & degenerative disease; USA: 2 million → 3.75 million (Harden, 2005)
- Chronic Pain – Complex mechanism, unsatisfied outcome, ↑ side effects
- The impact to patient → ↑ health care cost, ↓ daily activity, ↓ work productivity & quality of life

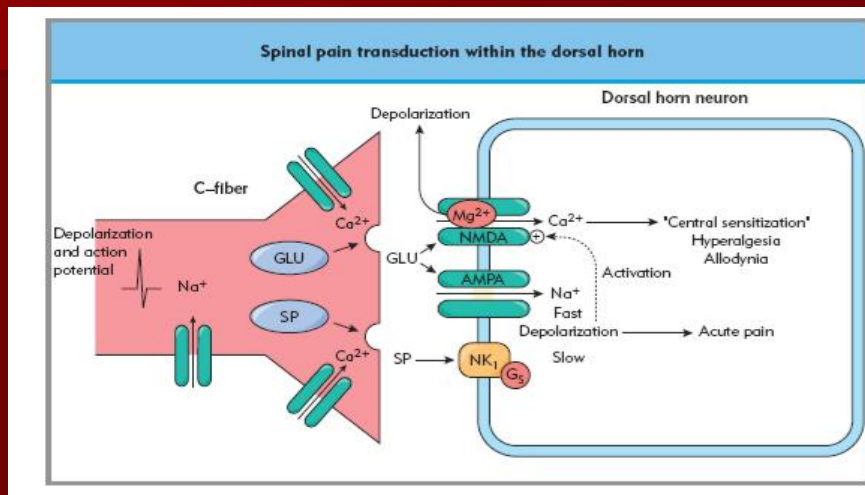
Pain transmission process (Hudspith, 2005)



Peripheral Sensitization (Hudspith, 2005)



Central Sensitization (Hudspith, 2005)



GLU: glutamat, SP: Substansi P

WHO Pain Analgesic Ladder

Mild Pain → NSAIDs or parasetamol



Moderate Pain → Opioid derivatives combine with paracetamol or NSAIDs



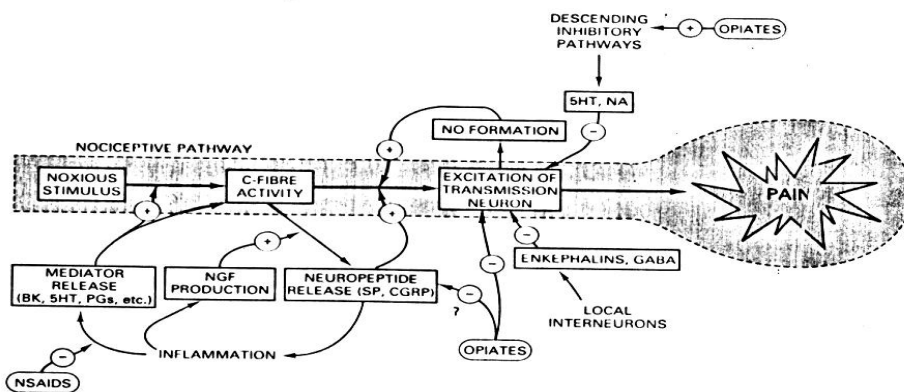
Severe Pain → High dose + adjuvant therapy

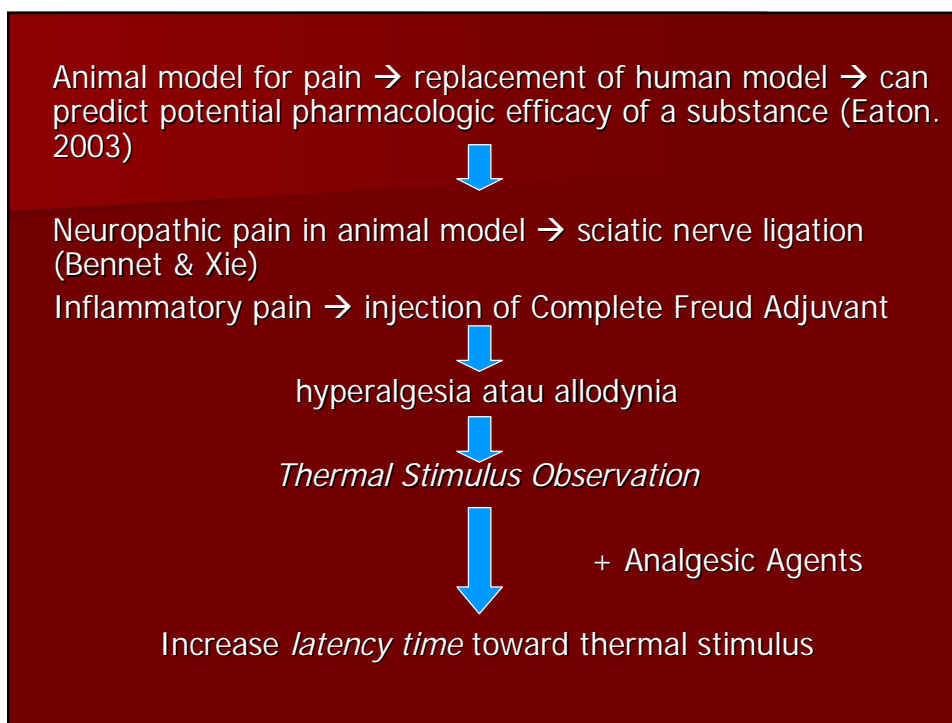
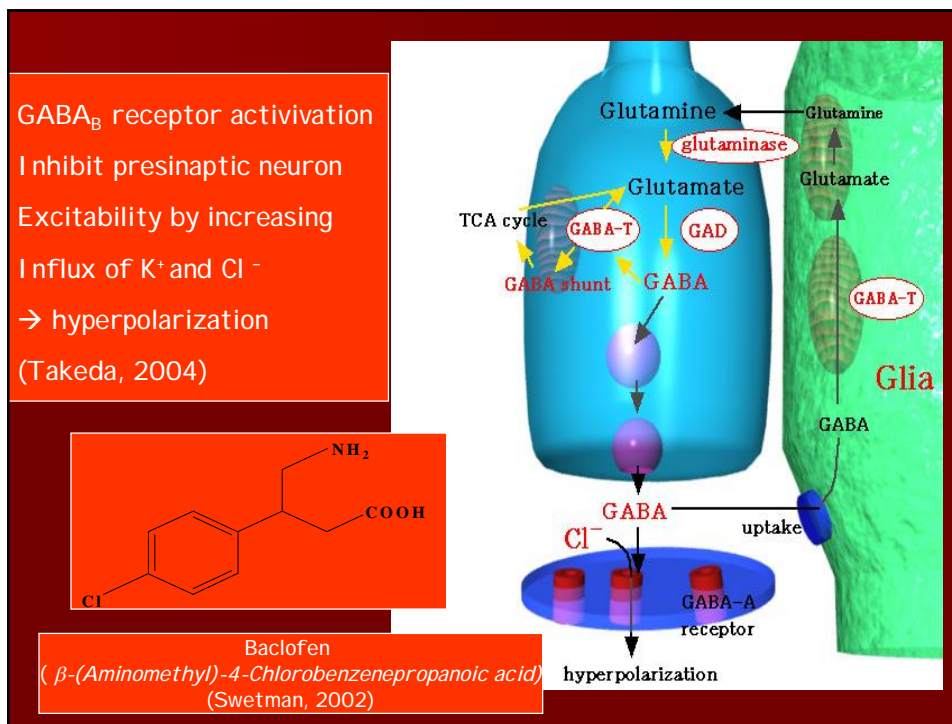


Unsatisfied output → Alternative strategy

Eg. Analgesic adjuvants at GABA-ergic system

Therapeutic Alternative → Involvement of GABA receptor

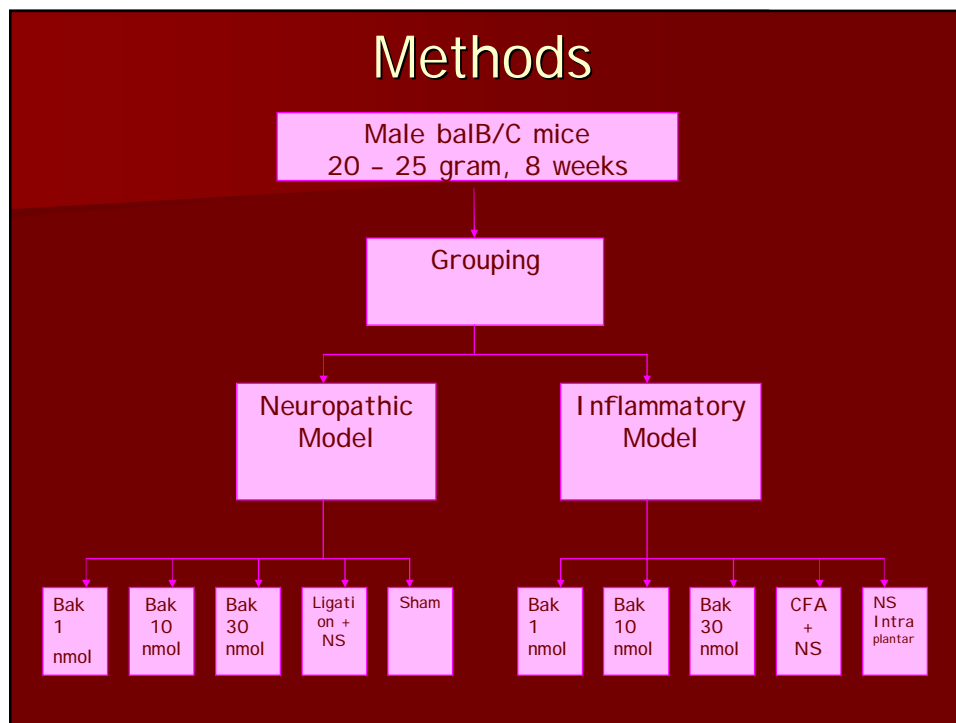


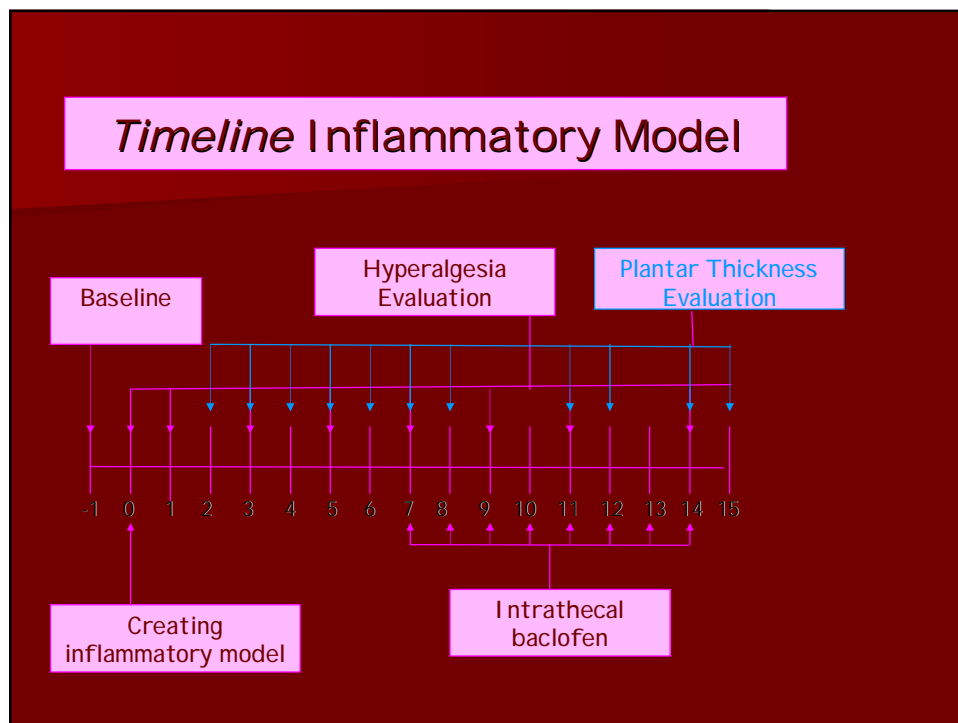
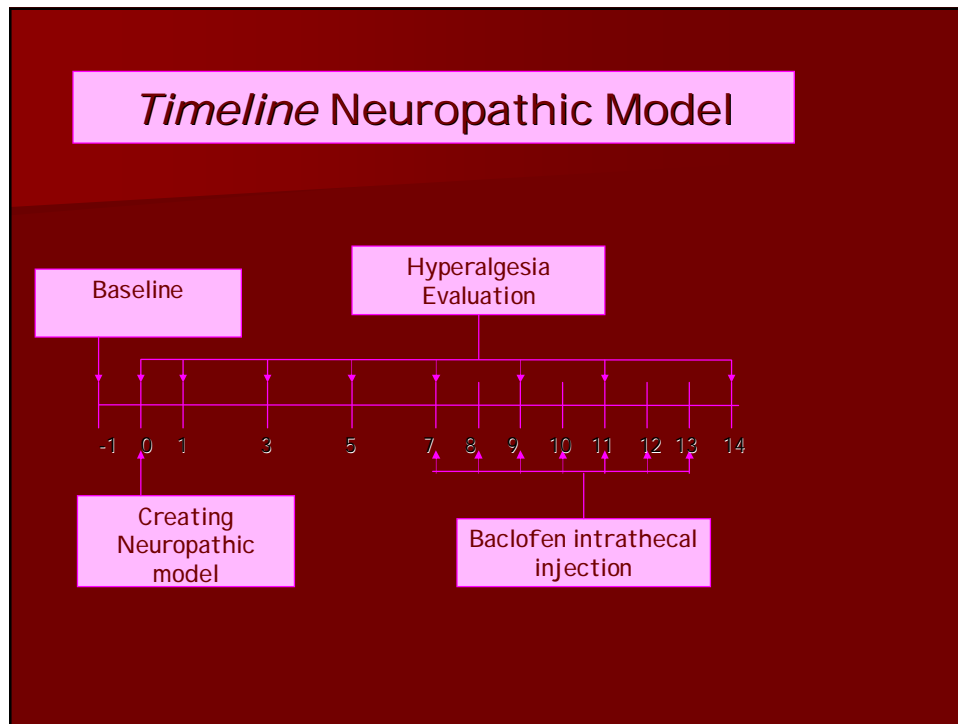


Objective

- To evaluate the effectiveness of GABA B agonist baclofen in the development of chronic pain either neuropathic or inflammatory pain

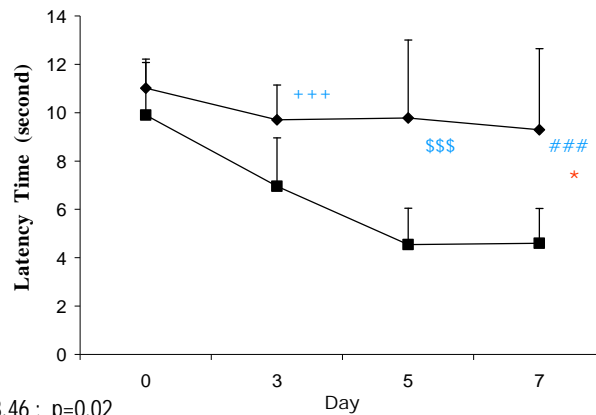
Methods





Results & Discussion

1. Neuropathic Pain



Legend:

* $F(1, 17) = 3.46$; $p=0.02$

+++ $p<0.01$

\$\$\$ $p<0.001$

$p<0.001$

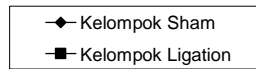


Figure 1. Development of neuropathic pain in mice

Table 1. Average Latency Time (second) toward Thermal Stimulation using *Hot Plate Test* in Neuropathic pain model

Group of Mice	Day						
	0	3	5	7	9	11	14
NS - Sham	11.01	9.69	9.78	9.29	10.05	11.19	11.98
Baclofen 1 nmol	11.92	6.67	5.74	4.80	5.11	7.49	9.85
Baclofen 10 nmol	9.57	7.56	4.90	4.52	6.27	9.73	10.92
Baclofen 30 nmol	9.17	7.19	3.88	4.76	7.98	8.57	9.22
NS - Ligation	8.17	6.23	3.17	4.13	5.85	5.57	4.71

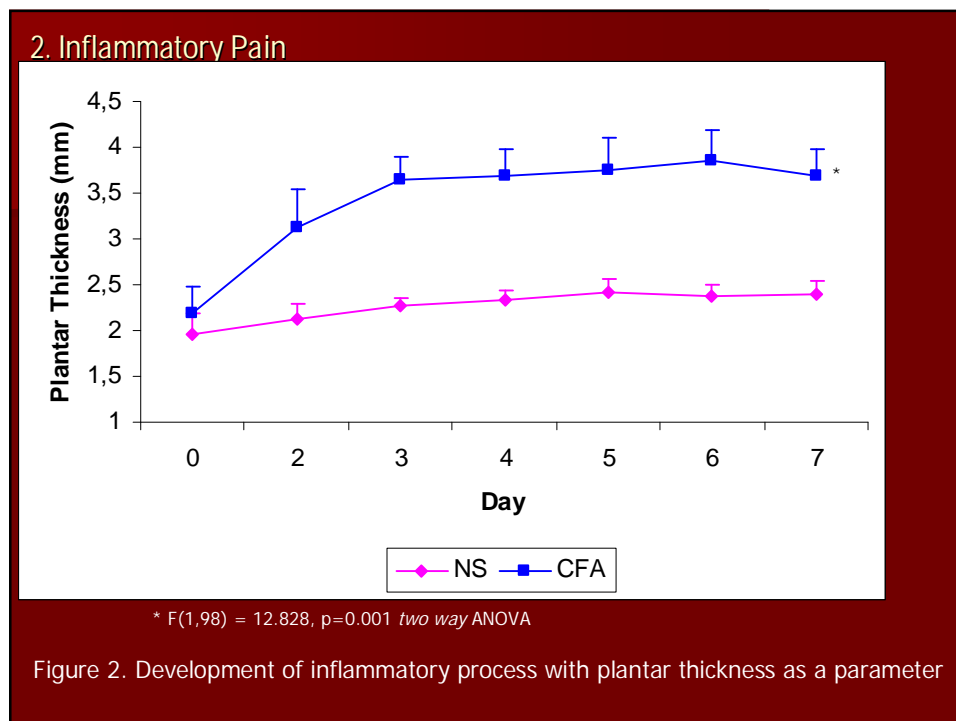
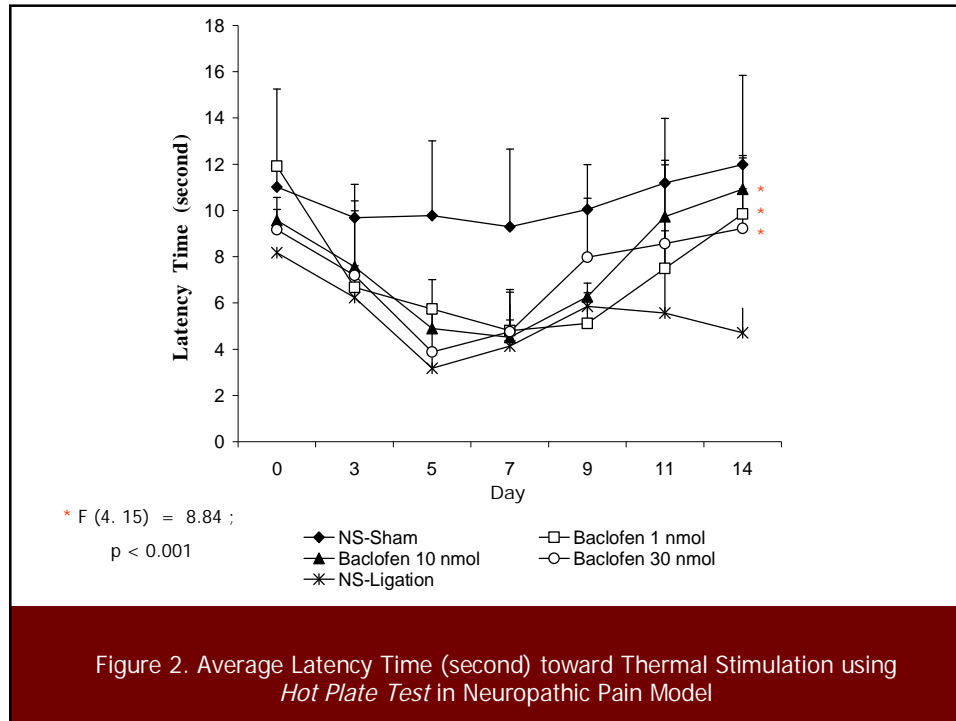
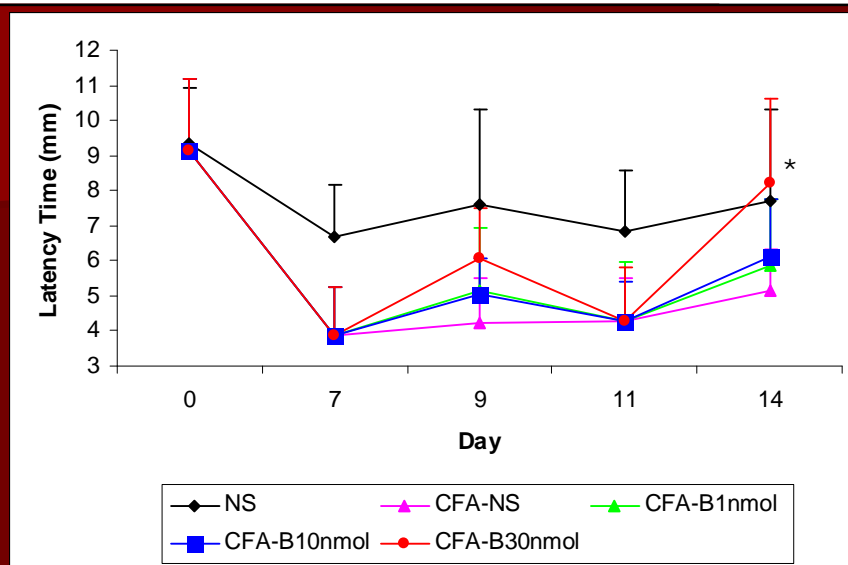


Table 2. Average latency time (second) toward thermal stimulation in inflammatory pain model

Group	Day					
	0	7	Treatment	9	11	14
NS	9.32	6.7	NS	7.58	6.81	7.69
CFA	9.12	3.89	NS	4.23	4.29	5.17
			B 1 nmol	5.14	5.37	5.86
			B 10nmol	5.05	5.42	6.12
			B 30nmol	6.07	6.91	8.24



* F (3,140) = 13.864, p = 0.001 two way ANOVA

Figure 3. Average latency time (second) toward thermal stimulation in inflammatory pain model

Conclusions

- Baclofen effective in managing chronic pain like state in mice

