

STUDY MECHANISM OF ACTION OF KRISHNA VAJRABHRAKA BHASMA (KVB) IN CHRONIC ASTHMA

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Asthma

- **Chronic inflammatory disorder**
- **Characterized by**
 - Hyper responsiveness of bronchi
 - Increased secretions
 - Mucosal edema
 - Mucosal plugging

Asthma

Acute

Chronic

Bronchospasm

Bronchospasm

Chr. Inflammation
& hyperactivity
of bronchi

Therapy of Acute Attack

Prophylactic therapy

Bronchodilators

Anti-inflammatory

Release of
mediators

(β_2 agonists)

(Corticosteroids)

(Mast cell stabilizers)

Limitations of asthma prophylaxis

- Corticosteroids:
(Effective but many adverse effects)
- Mast cell stabilizers:
(Less adverse effects but less effective)
- So, search continues:
For a new, effective and safe drug.

Krishna Vajrabhraka Bhasma (KVB)

- An ayurvedic preparation
- Used very commonly to reduce frequency of acute asthmatic attacks in chronic asthma (> one year duration)
- ‘Mica’ (abhraka) main constituent of KVB
- Efficacy and exact mechanism of action: Not known.

Krishna Vajrabhraka Bhasma

- **Source:** College of Ayurveda, BVDU, Pune.
- **Studies conducted by us:**

➤ **Toxicity Testing:**

- **Acute:** OECD guideline 420

$LD_{50} > 2000\text{mg/kg}$.

- **Subacute:** OECD guideline 423

No toxicity up to 50mg/100gm

(Four times human dose)

Krishna Vajrabhraka Bhasma

- **Studies conducted by us...**

- **Efficacy testing:**

- Bronchial hyper reactivity in Guinea pigs:

- Egg albumin aerosol in Histamine Chamber

- Corticosteroid- positive control

- Parameter used- pre convulsive time

- Result: KVB efficacy comparable to Corticosteroids

AIM

To study the mechanism of action of KVB in Chronic Asthma.

OBJECTIVES

- 1.To study the effect on Mast cell degranulation.
- 2.To study Anti – inflammatory activity.

Material



and



Methods

Exp I - Mast Cell Stabilization in Rats

- Animals:
 - Albino Rats
 - Either sex
 - Weight-150 to 200 gms.
- Sensitization:
 - With egg albumin (20 mg I.P. & 20 mg S.C.)
 - Sensitization period - 21 days
- Treatment: given as per group.
 - Animals divided into 5 groups of 6 animals each.
- KVB dose: extrapolated from human dose
 - 11mg/ 100gm rat - Low dose
 - 22mg/100gm rat - High dose

Mast Cell Stabilizing Activity

Studied in 2 parts:

- Part A: Single dose treatment
(3 hrs before challenge)
- Part B: Sub-acute treatment
(daily for 14 days before challenge)

Mast Cell Stabilizing Activity - Part A (SD)

Group No.	Treatment	Route	Interval before challenge
(I)	Vehicle Control (honey)	Oral	3hrs SD
(II)	Vehicle Control (water)	Oral	3hrs SD
(III)	KVB low dose (11mg/100gm)	Oral	3hrs SD
(IV)	KVB high dose (22mg/100gm)	Oral	3hrs SD
(V)	Sodium cromoglycate (0.25mg/100gm)	Intraperitoneal	SD 30 min. before challenge

Mast Cell Stabilizing Activity - Part B

Group No.	Treatment (dose)	Route	Duration
(I)	Vehicle Control (honey)	Oral	14 days
(II)	Vehicle Control (water)	Oral	14 days
(III)	KVB low dose (11mg/100gm)	Oral	14 days
(IV)	KVB high dose (22mg/100gm)	Oral	14 days
(V)	Sodium cromoglycate (0.25mg/100gm)	Intraperitoneal	SD 30 min. before challenge

...Mast Cell Stabilization in Rats

● Challenge: Egg albumin 20 mg I.P. to all animals .

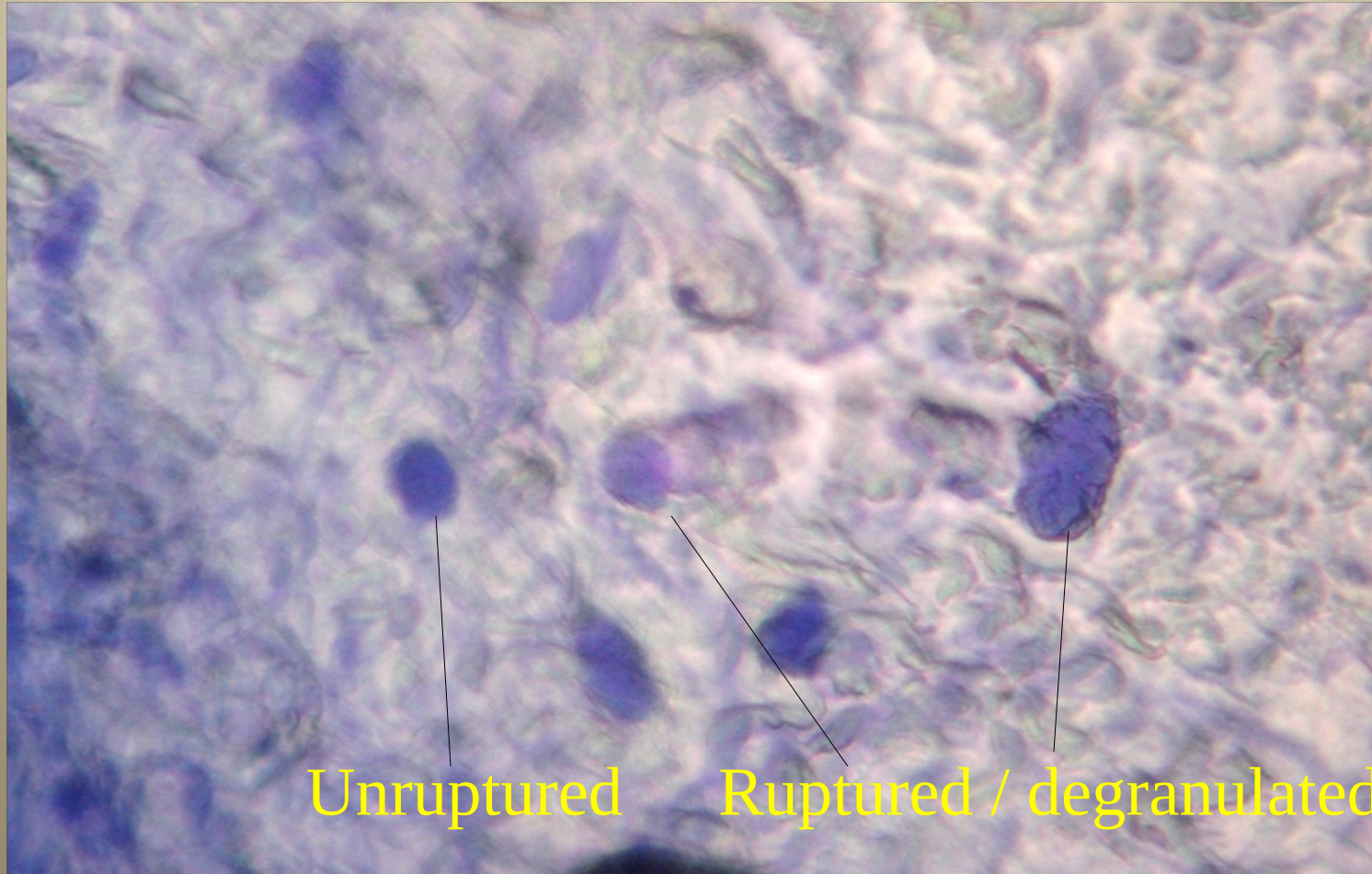
● Collection of Mesentery:

- Animals sacrificed 30 min after challenge
- Mesentery collected in 10% formalin

● For Observation:

- Each piece of mesentery stained with toluidiene blue
- Placed over a neubaur chamber
- Number of mast cells (Ruptured & Unruptured) counted under high power (40X) microscope.

Mast Cells in mesentery



Parameter : Percentage of unruptured mast cells

Exp II- Anti-inflammatory action in Rats

Animals:

- Albino Rats
- Either sex
- Weight-150-200 gms.

Model: – Granuloma Pouch Technique

1st Day – Preparation of Air pouch (20ml of air) on the dorsum between shoulder limbs.

2nd Day – Inj. of 0.5ml croton oil in sesame oil.

3rd Day – Air withdrawn, adhesions broken.

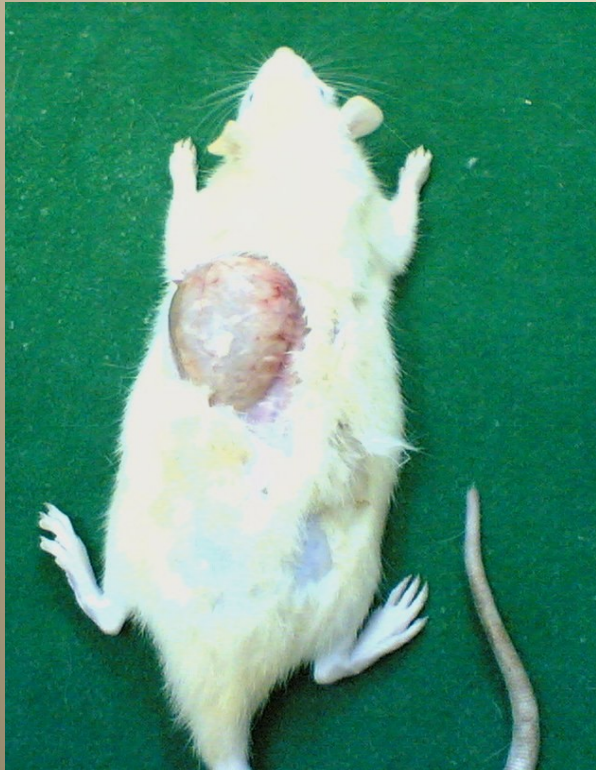
3rd – 9th Day – Treatment given as per group.

Anti-inflammatory activity

Group No.	Treatment(dose) 3 rd to 9 th day	Route	Duration
(I)	Vehicle Control (Honey)	Oral	7days
(II)	Vehicle Control (Water)	Oral	7days
(III)	KVB Low dose (11mg/100gm)	Oral	7days
(IV)	KVB High dose (22mg/100gm)	Oral	7days
(V)	Diclofenac sodium (10mg/kg)	Oral	7days

10th Day – Pouch dissected, weighed, exudate measured.

Granuloma Pouch



In Vivo

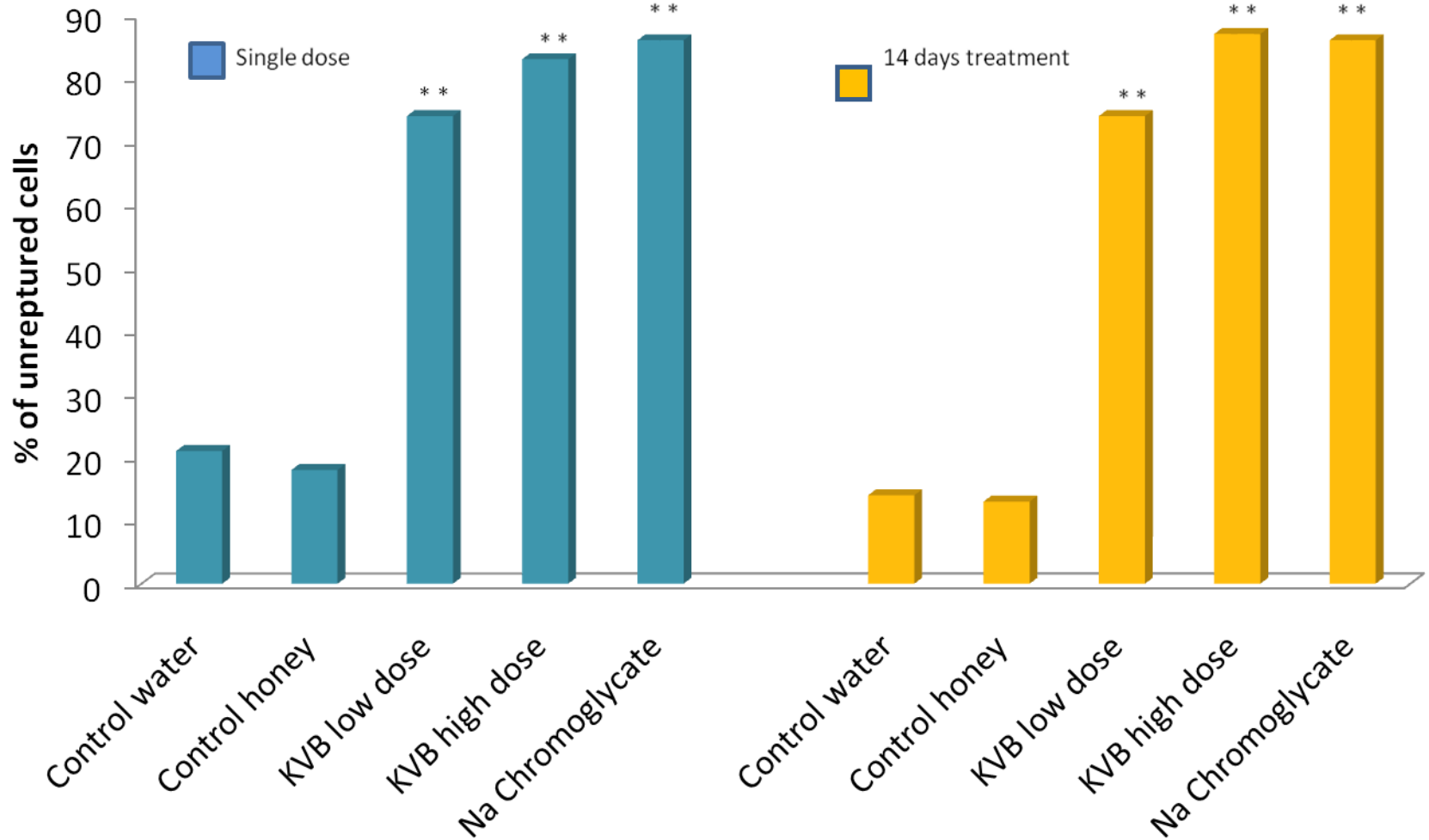


In Vitro

Parameter : **‘Weight of Pouch’ & ‘Amount of Exudate’**

Results

Exp. I- Mast cell stabilization in rats Comparison between KVB single dose & 14 days treatment

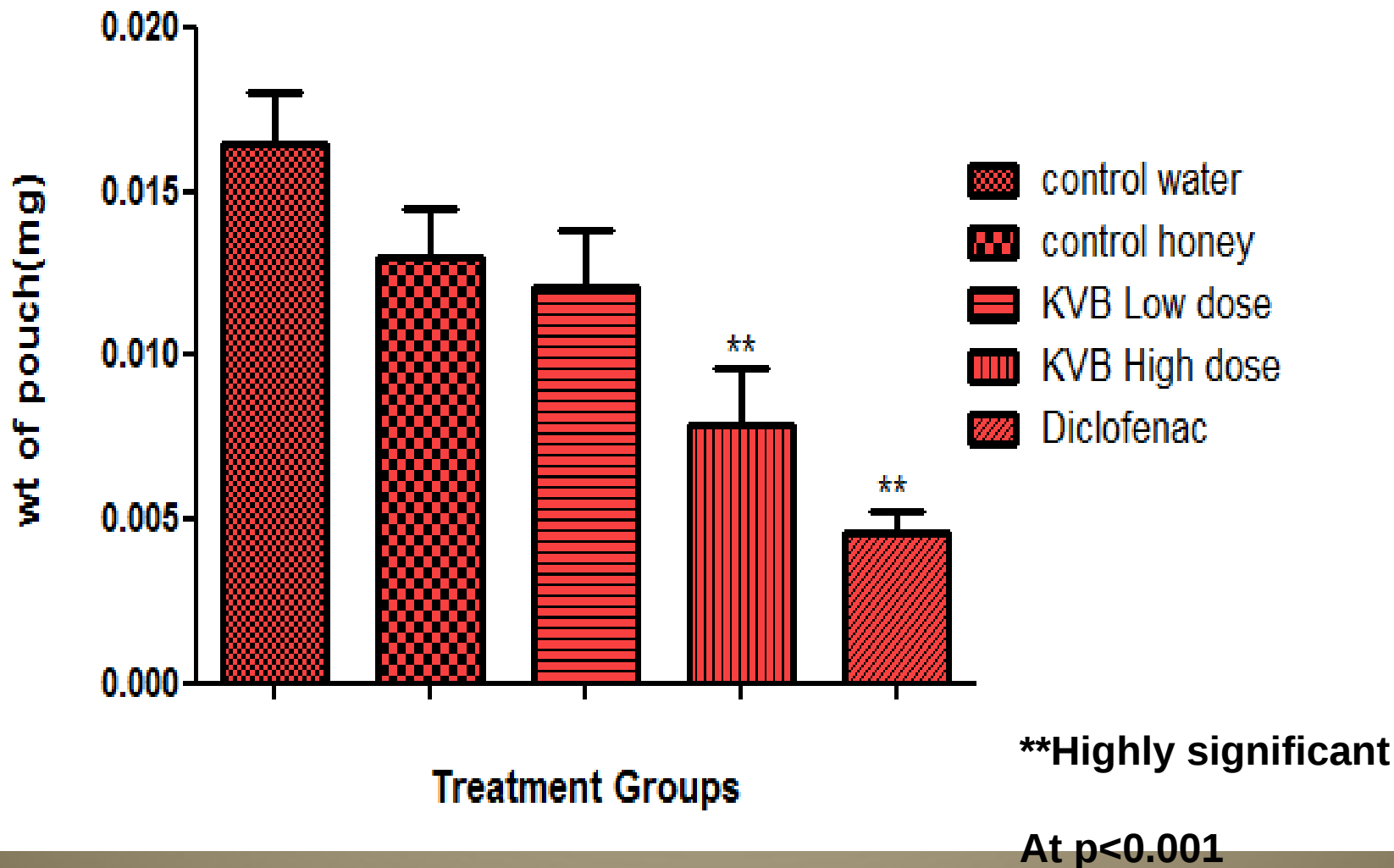


**** Highly significant $p < 0.001$**

Treatment Groups

Results

Exp. II Anti-inflammatory action

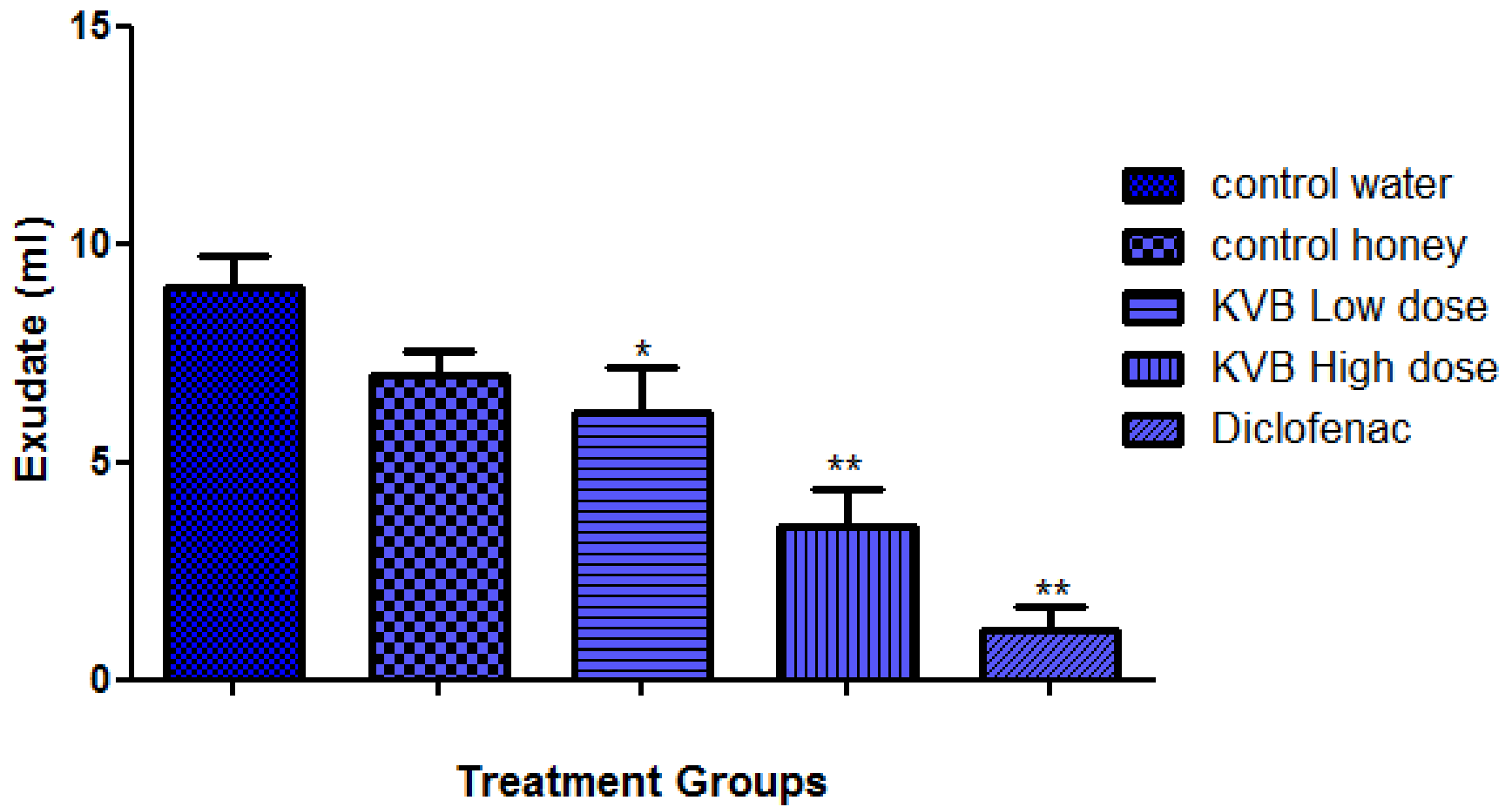


**Highly significant

At p<0.001

Results

Exp. II Anti-inflammatory action

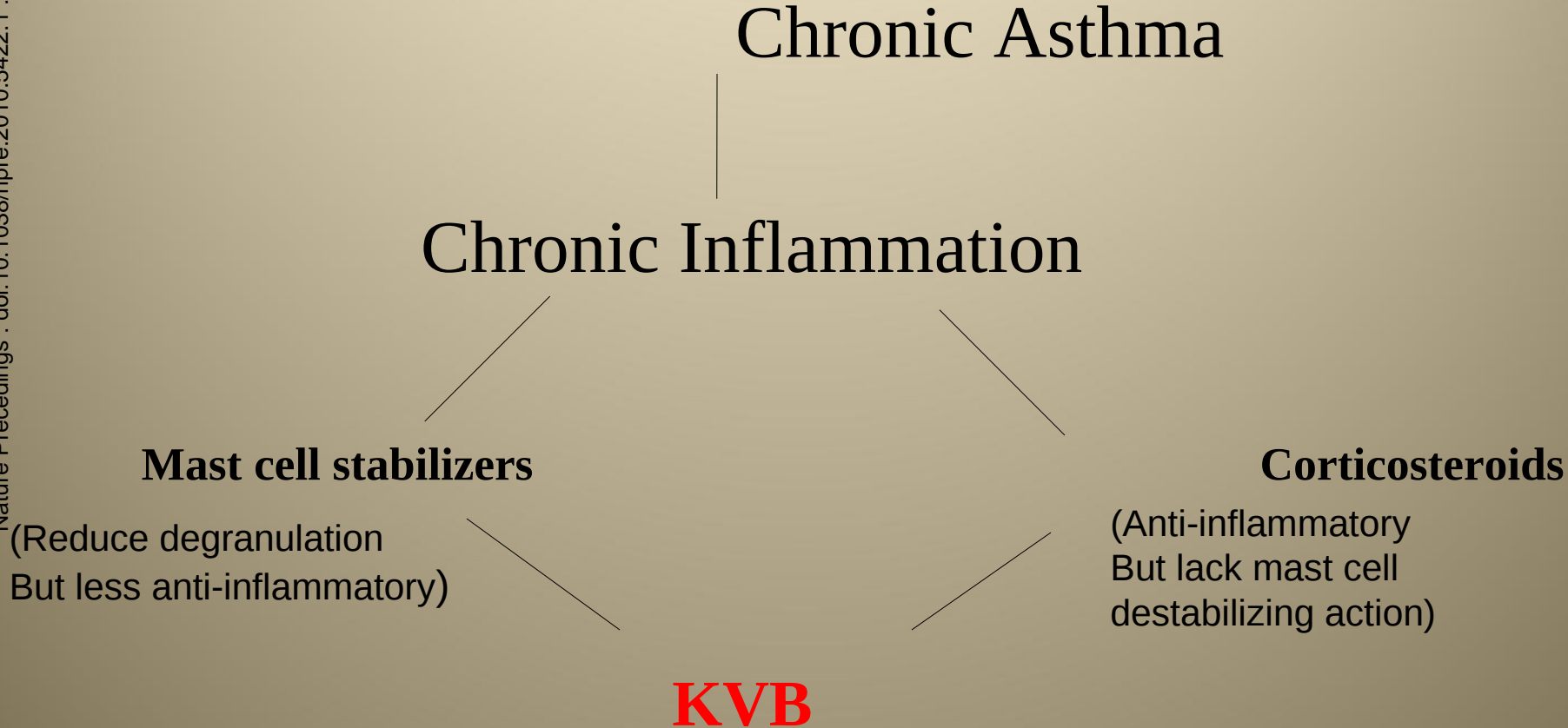


** Highly significant at $p < 0.001$

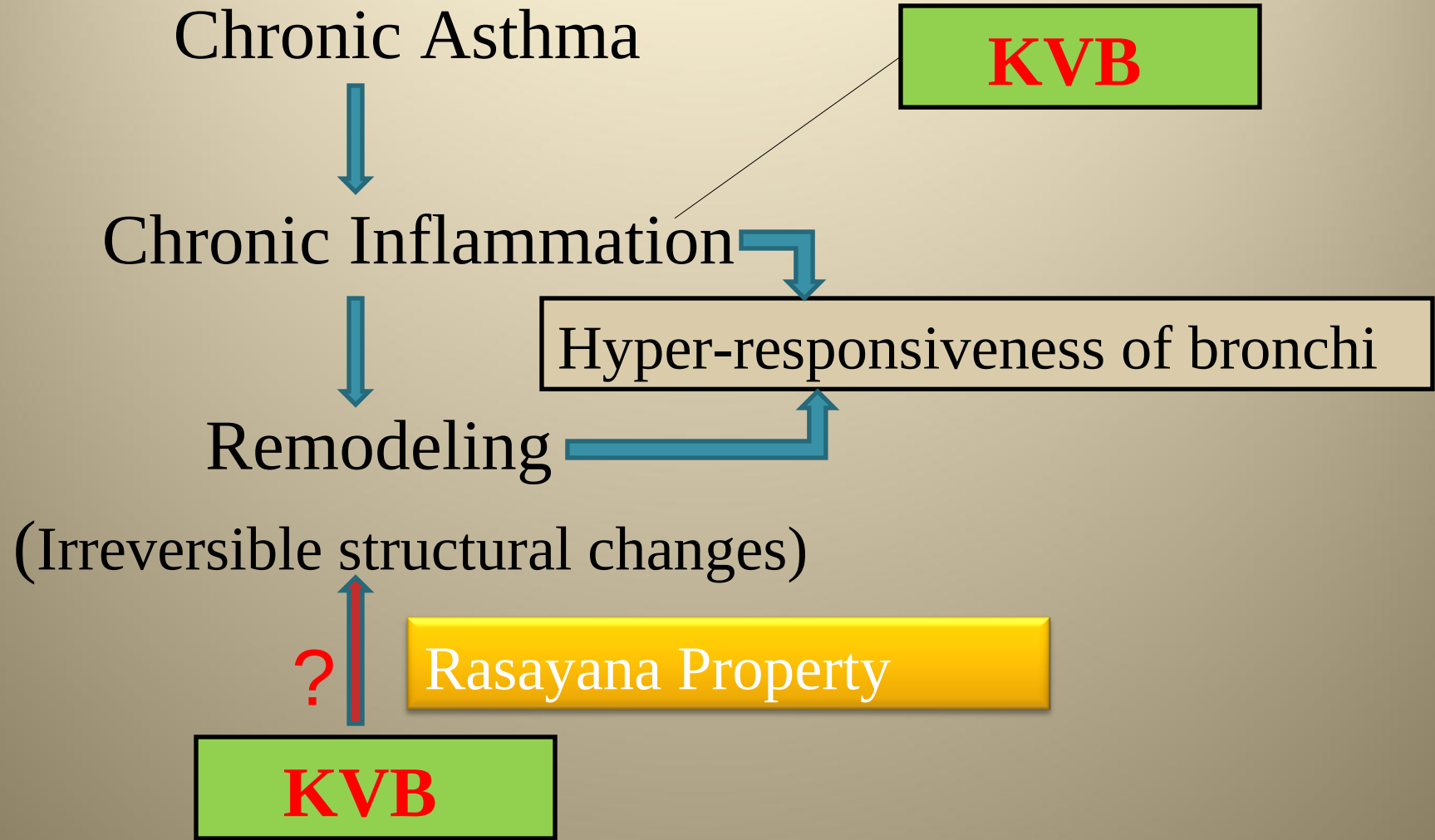
Discussion

KVB, an ayurvedic preparation, is used to prevent acute attacks in chronic asthma.

Nature Precedings : doi:10.1038/npre.2010.5422.1 : Posted 21 Dec 2010



Future Studies



Study the effect of KVB on bronchial remodeling

THANK
YOU

Classification of Abhraka

According to colors

- Sweta (White)
- Rakta (Red)
- Peeta (Yellow)
- Krishna (Black)

According to effect of heat:

- Pinak Abhraka
- Nag Abhraka
- Manduka Abhraka
- Vajra Abhraka

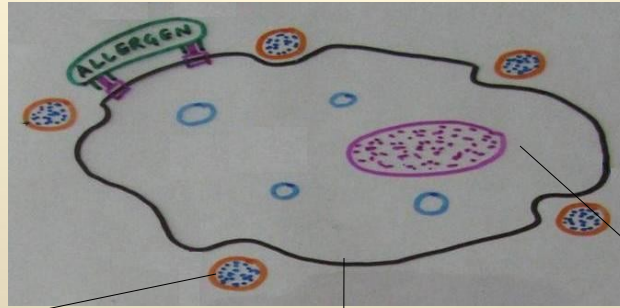
Krishna Vajrabhrak

Preparation of Krisnna vajrabhraka Bhasma

Steps to obtain bhasma

- **Shodhan**
Detoxification
- **Dhanybhraka Nirman:**
Intermediate step to reduce particle size
- **Maran**
Conversion to lusterless light weight smooth fine powder.

Toxicity studies



Degranulation
(immediate)
Histamine, Heparin,
Proteases, TNF α

Membrane derived
mediators
(over min.)
PGs,
Leukotrienes, PAF

Cytokine production
(over Hrs.)
Interleukins

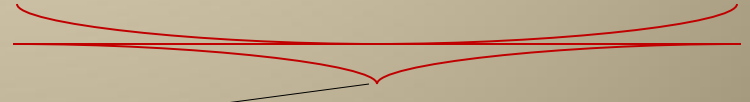
Bronchoconstriction

Vasodilatation

Influx of inflammatory cells

Synthesis & release of mediators

Sm. Muscle hyper reactivity



Expt. I A: % Unruptured cells (S.D. treatment)

NO.	CONTROL HONEY	CONTROL WATER	III KVB Low dose	IV KVB high Dose	V Na cromoglycate
1	17.74	13.74	75	87.03	81.45
2	20.31	18.2	68.42	82.35	87.78
3	23.89	17.58	75	86.27	85.12
4	20.31	21.06	69.7	80.77	91.3
5	20.54	18.5	73.33	76.32	87.78
6	24.24	20.46	84.44	88.44	84.44
MEAN ± SD	21.17 ±2.37	18.27 ±2.07	74.32 ** ±2.4	86.31** ±1.42	83.53** ±9.5

** significantly more effective (P<0.05)

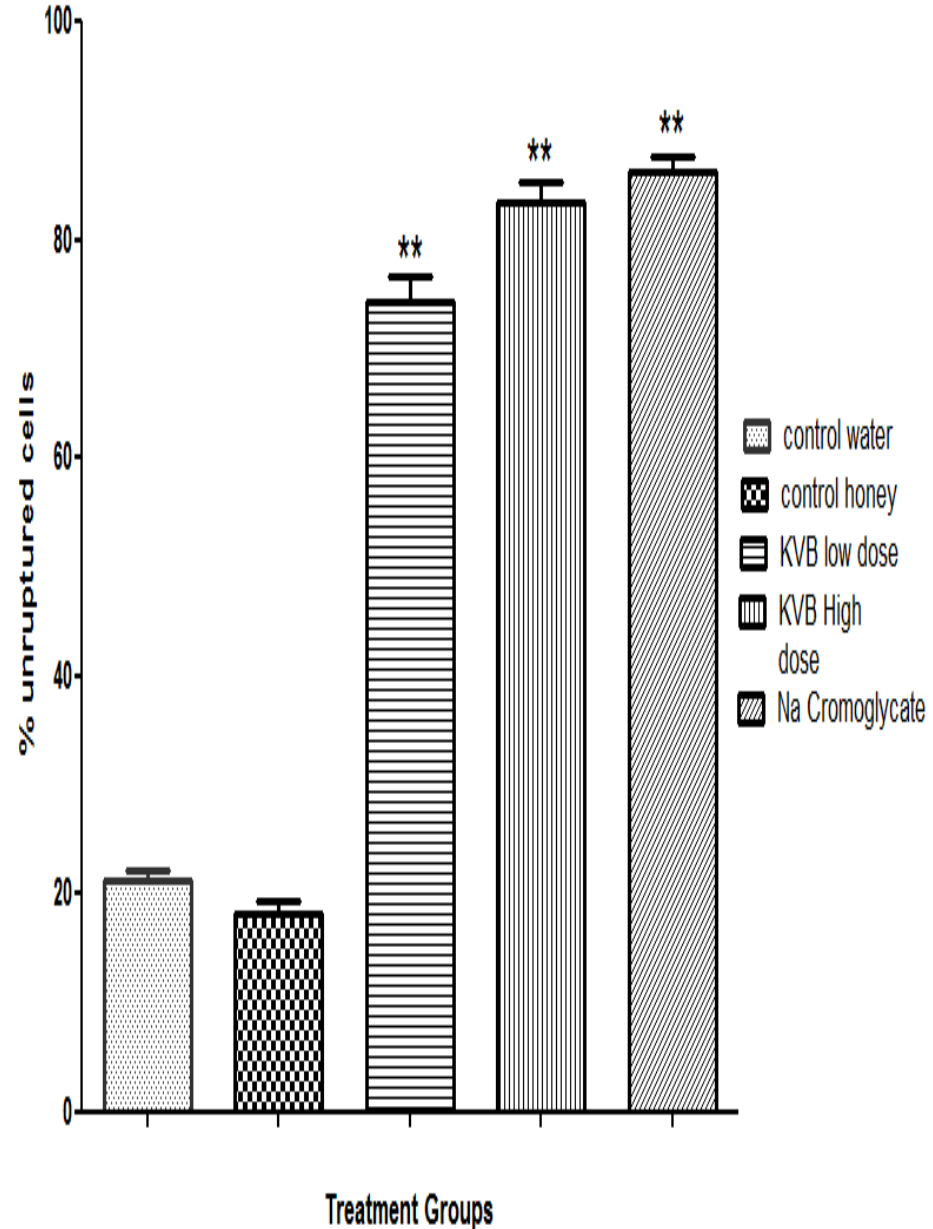
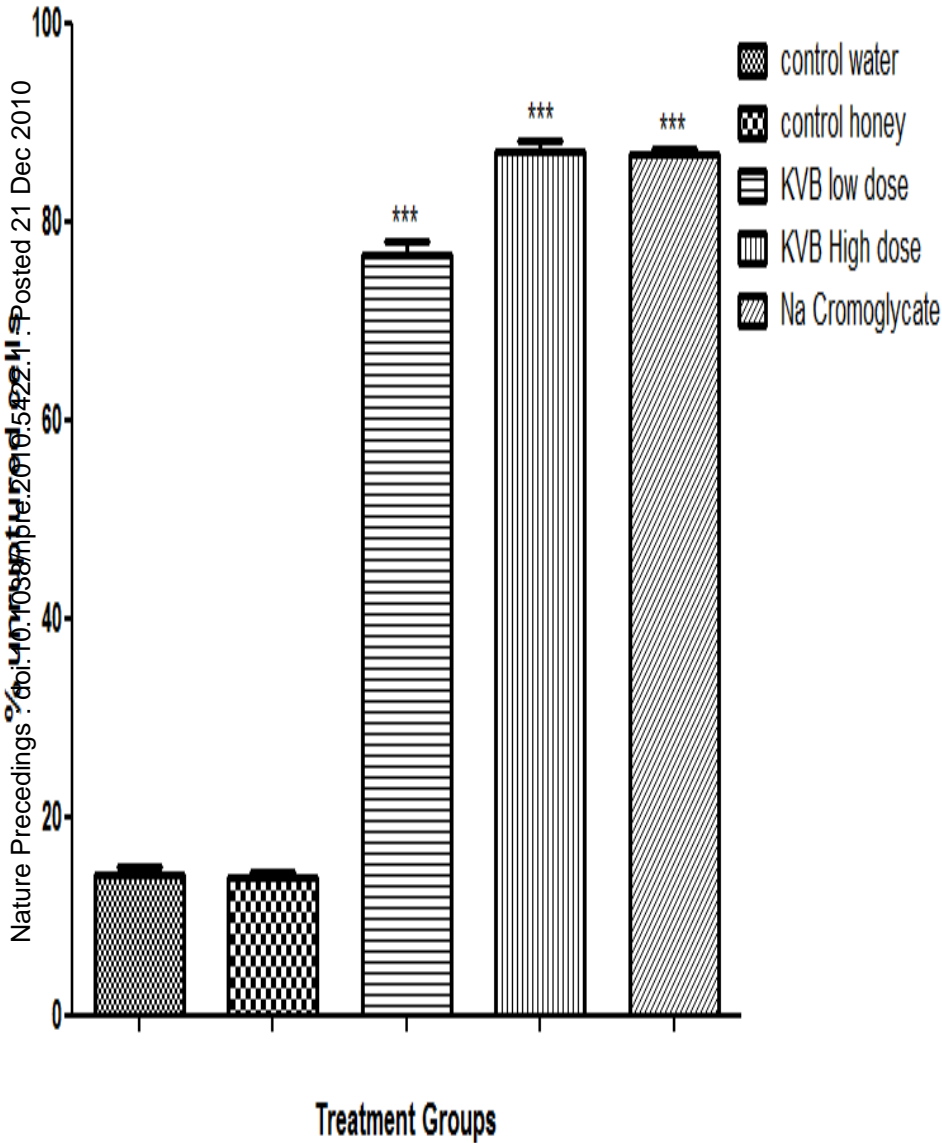
Expt.IB: % Unruptured cells (Chronic Pretreatment)

NO.	CONTROL HONEY	CONTROL WATER	III KVB Low dose	IV KVB high Dose	V Na cromoglycate
1	13.72	13.42	80.35	85.93	88.33
2	17.85	16.32	78.57	88.88	87.75
3	13.55	13.55	79.03	89.65	87.87
4	12.72	13.72	76.13	88.46	85.24
5	14.28	13.88	74.62	82.69	87.5
6	13.24	12.56	71.18	86.66	84.44
MEAN ± SD	14.22 ±5.9	13.90 ±5.9	74.64** ±4.74	86.55** ±4.7	87.04** ±2.37

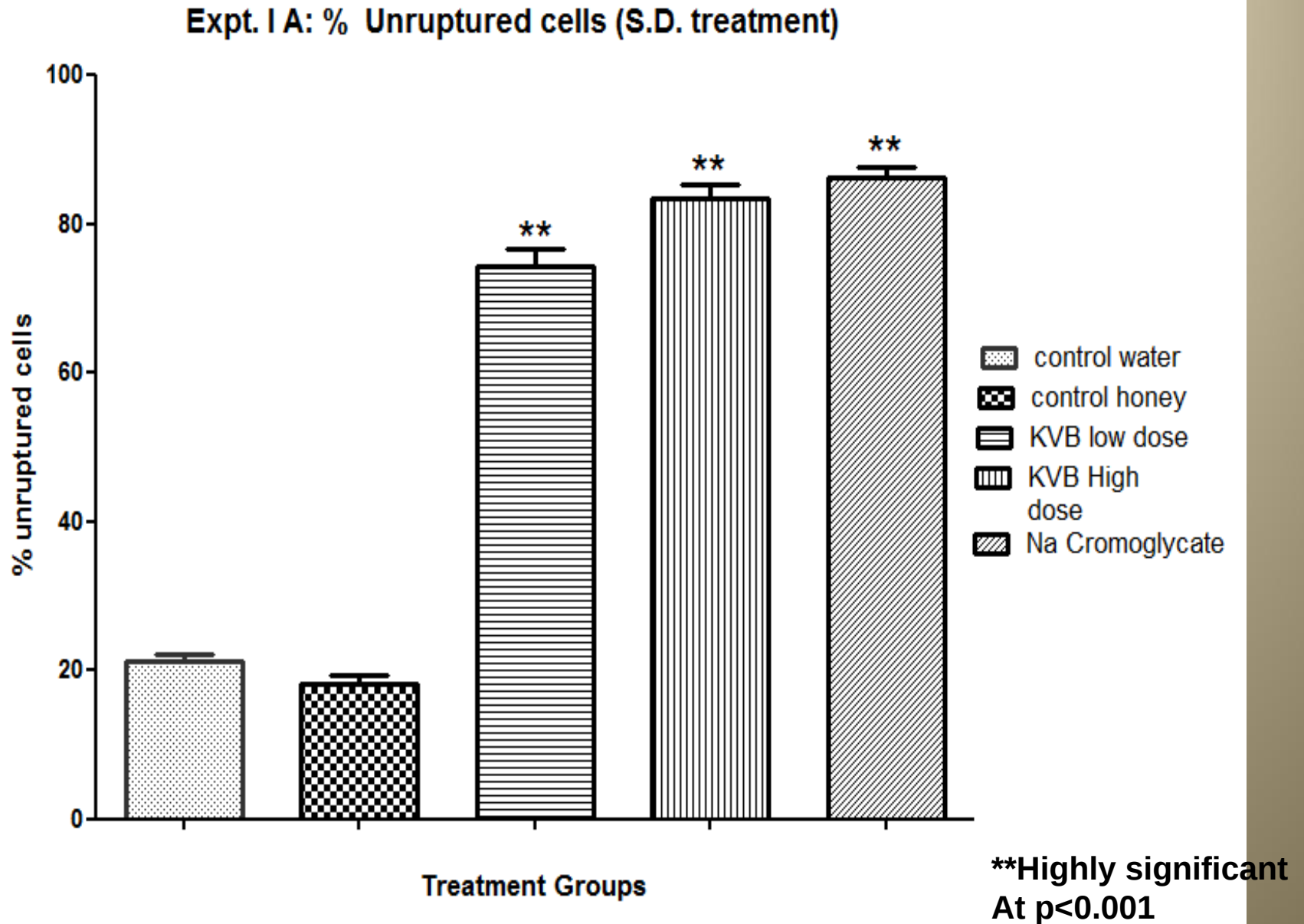
** significantly more effective (P<0.05)

Expt. I B: % Unruptured cells (Chronic Pretreatment)

Expt. I A: % Unruptured cells (S.D. treatment)

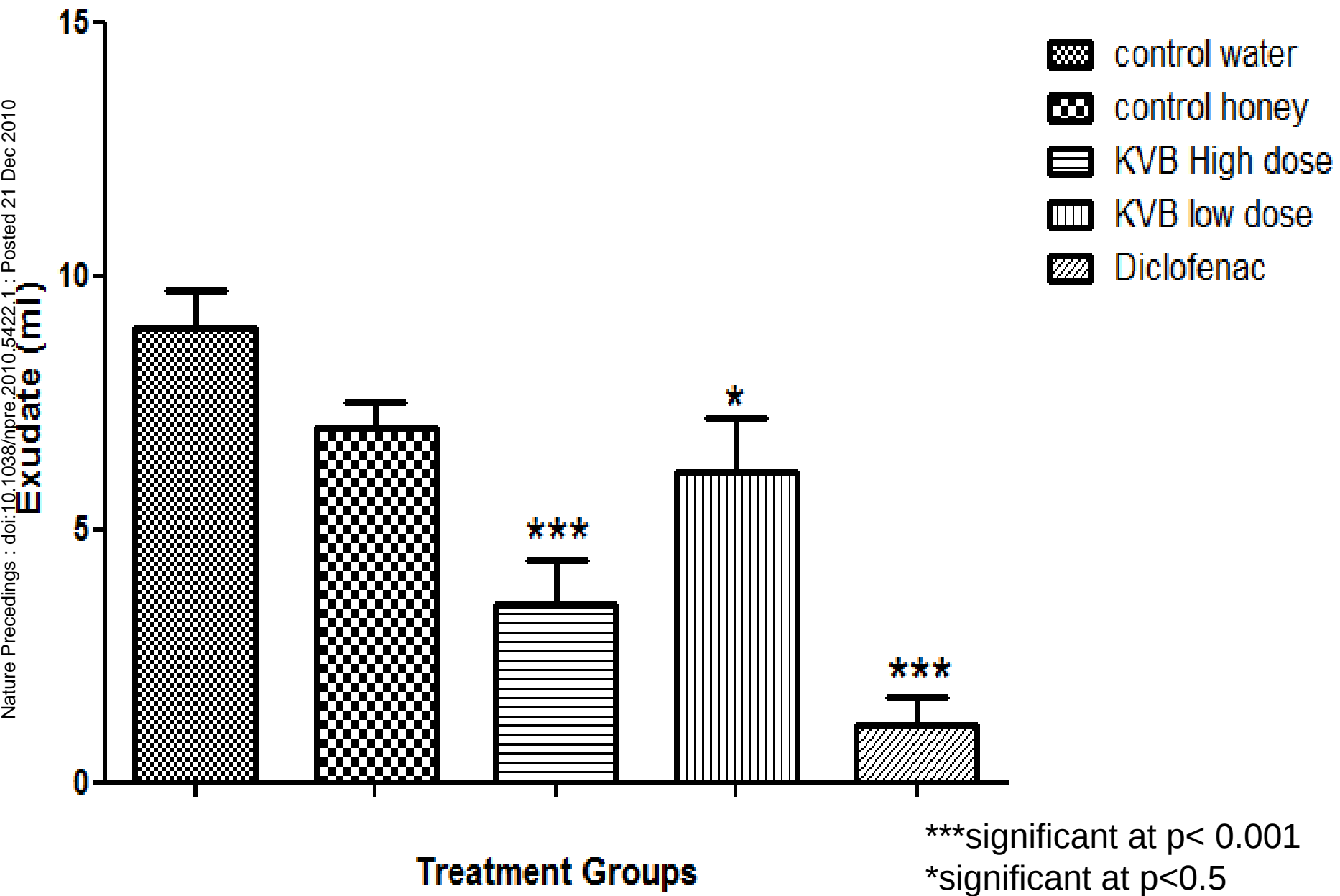


Results

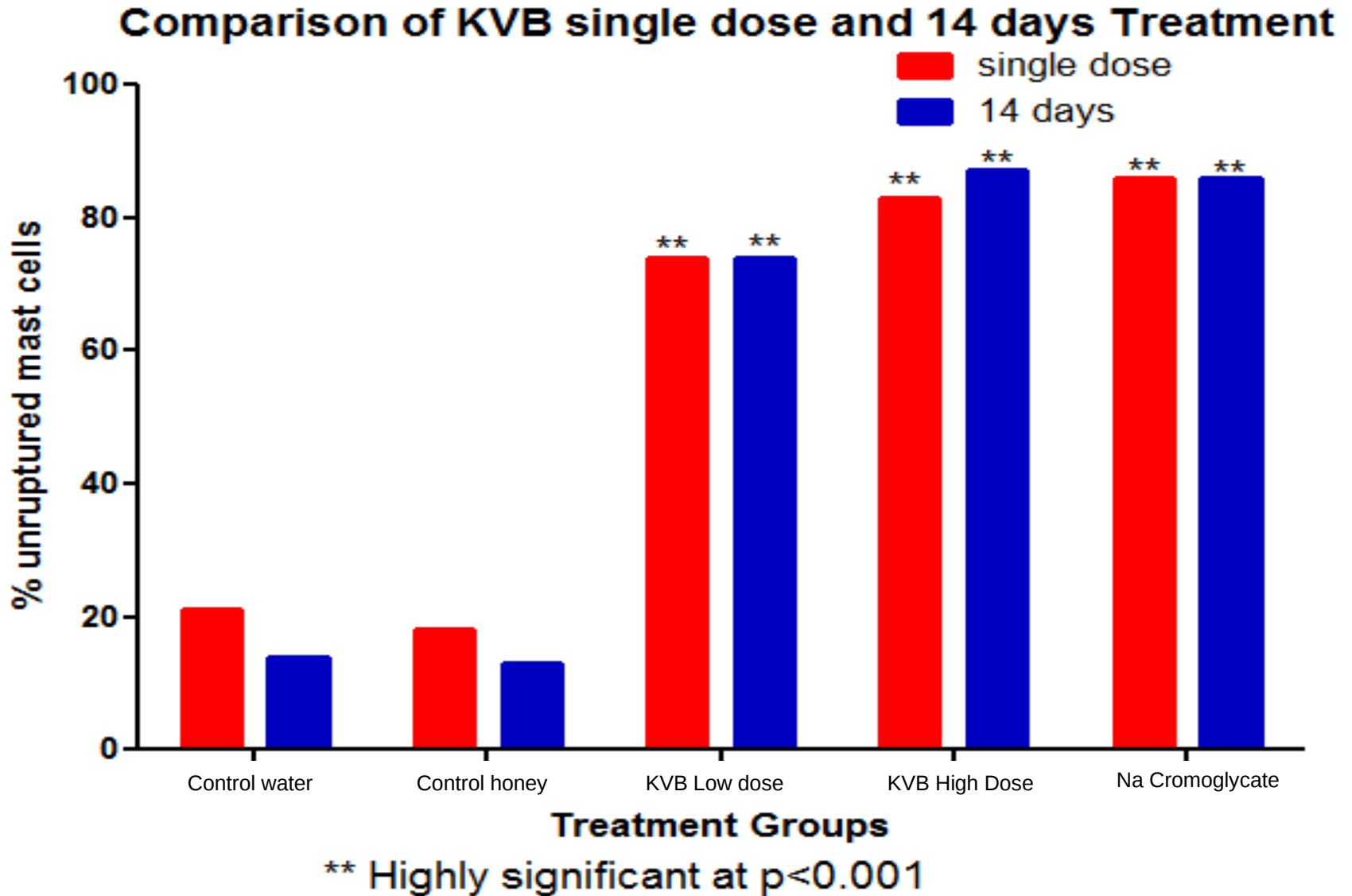


Exp. II Anti-inflammatory action

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Results



Results

Comparison between KVB single dose & 14 days treatment

