About OMICS Group

OMICS Group is an amalgamation of Open Access Publications and worldwide international science conferences and events. Established in the year 2007 with the sole aim of making the information on Sciences and technology 'Open Access', OMICS Group publishes 500 online open access scholarly journals in all aspects of Science, Engineering, Management and Technology journals. OMICS Group has been instrumental in taking the knowledge on Science & technology to the doorsteps of ordinary men and women. Research Scholars, Students, Libraries, Educational Institutions, Research centers and the industry are main stakeholders that benefitted greatly from this knowledge dissemination. OMICS Group also organizes 500 International conferences annually across the globe, where knowledge transfer takes place through debates, round table discussions, poster presentations, workshops, symposia and exhibitions.

OMICS International Conferences

OMICS International is a pioneer and leading science event organizer, which publishes around 500 open access journals and conducts over 500 Medical, Clinical, Engineering, Life Sciences, Pharma scientific conferences all over the globe annually with the support of more than 1000 scientific associations and 30,000 editorial board members and 3.5 million followers to its credit.

OMICS Group has organized 500 conferences, workshops and national symposiums across the major cities including San Francisco, Las Vegas, San Antonio, Omaha, Orlando, Raleigh, Santa Clara, Chicago, Philadelphia, Baltimore, United Kingdom, Valencia, Dubai, Beijing, Hyderabad, Bengaluru and Mumbai.

Medicinal application of potassium humate

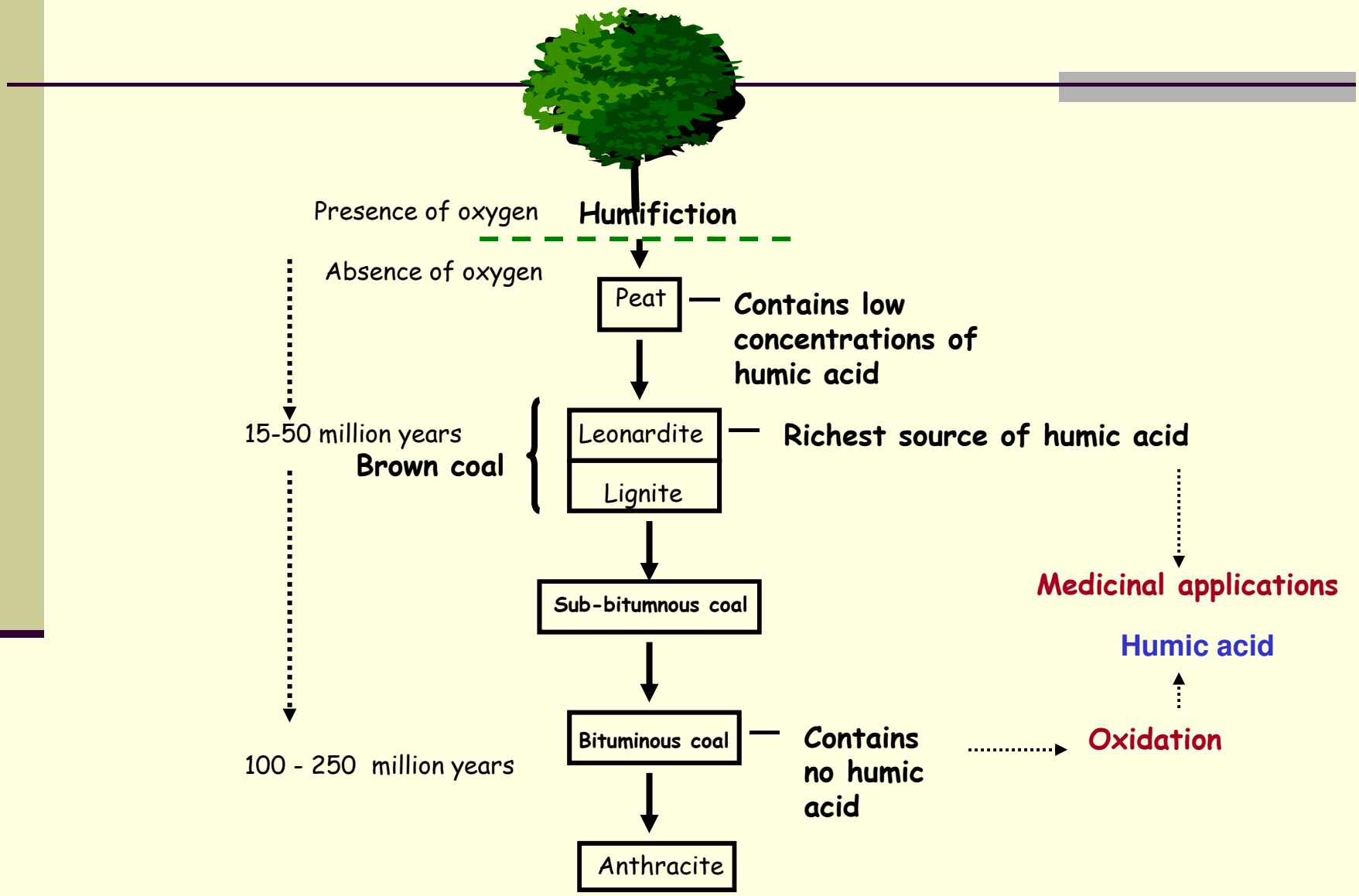
Connie Medlen (C.E.J. van Rensburg)
University of Pretoria, South Africa

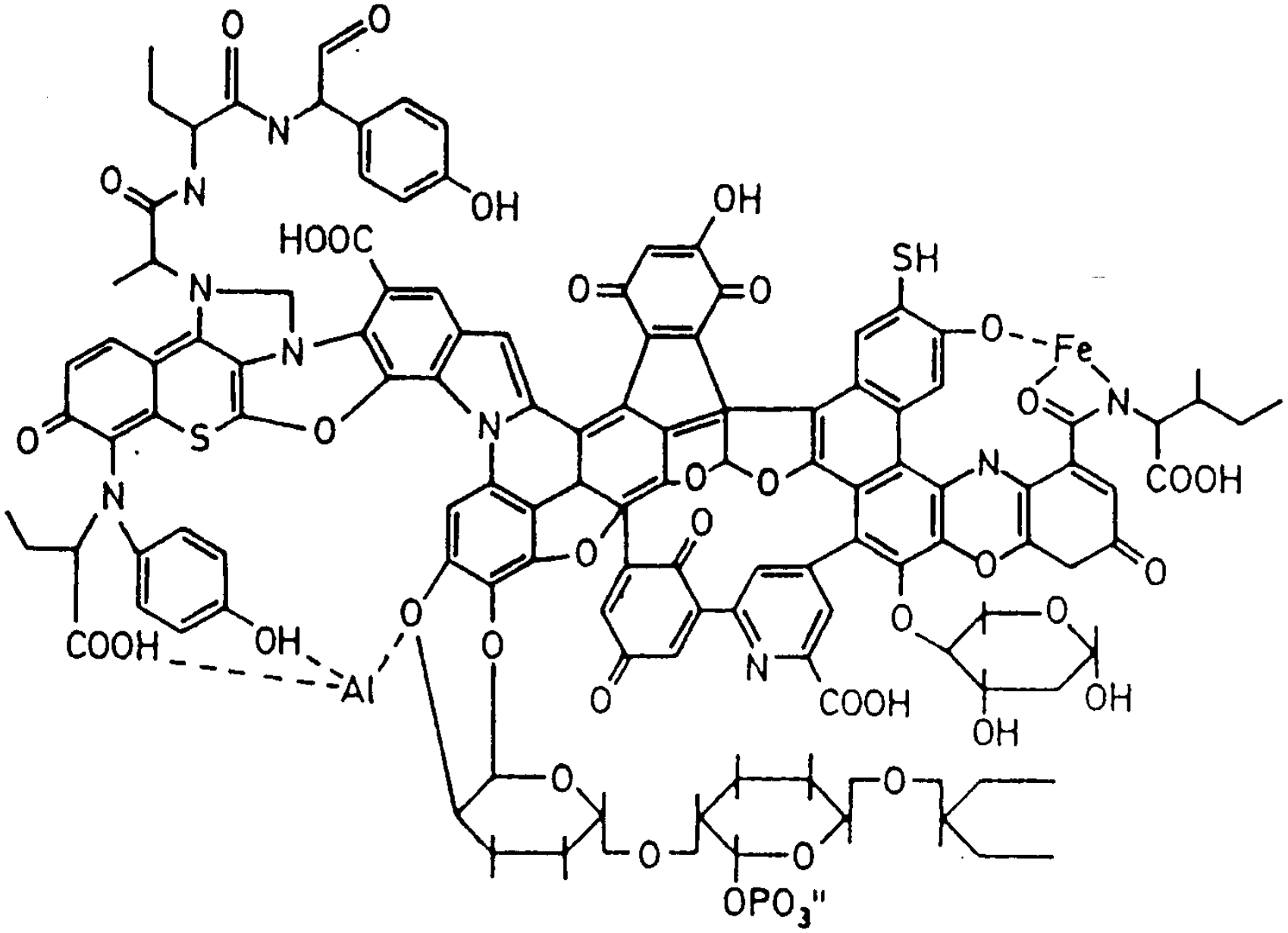
- Humic substances are formed during the decomposition of plant material.

- In the past there has been indications in literature, mostly anecdotal, that it possesses medicinal applications.

- Arthritic sufferers used to lie in mud baths to relieve their symptoms

Formation of humic acids and coal




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ENERKOM was founded

- Dr Dekker, a chemist, was tasked, by the SA government, to find other applications for bituminous coal (except burning).

- He developed an oxidation process to convert bituminous coal to potassium humate.

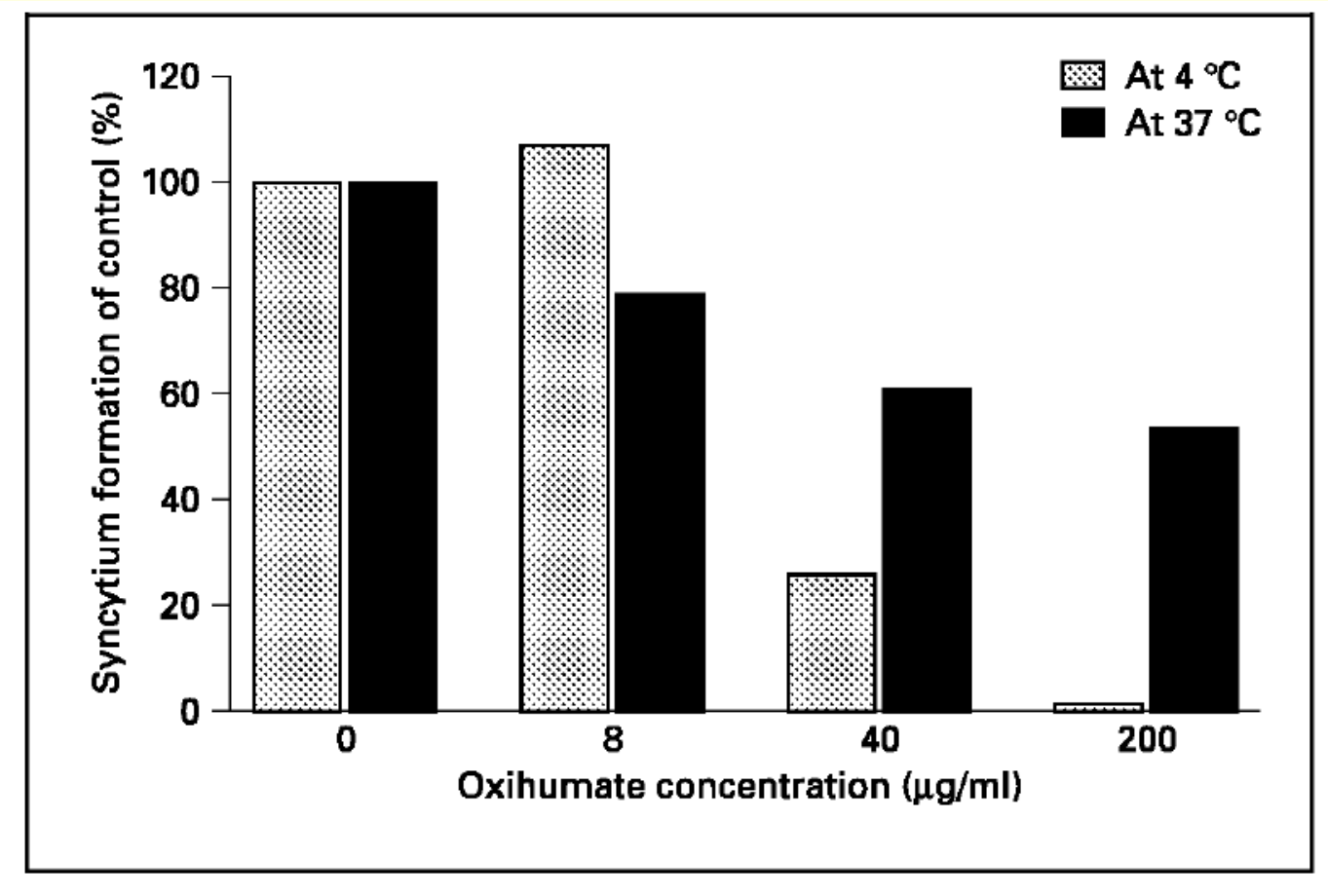
- He arrived in my office (Dept of Immunology, University of Pretoria) with a sample – which he called oxihumate.

- **All he wanted to do is test it for activity against the HIV virus.**

- **this was at the beginning of the AIDS epidemic (2001-2002)**

- **there was still no treatment for AIDS**

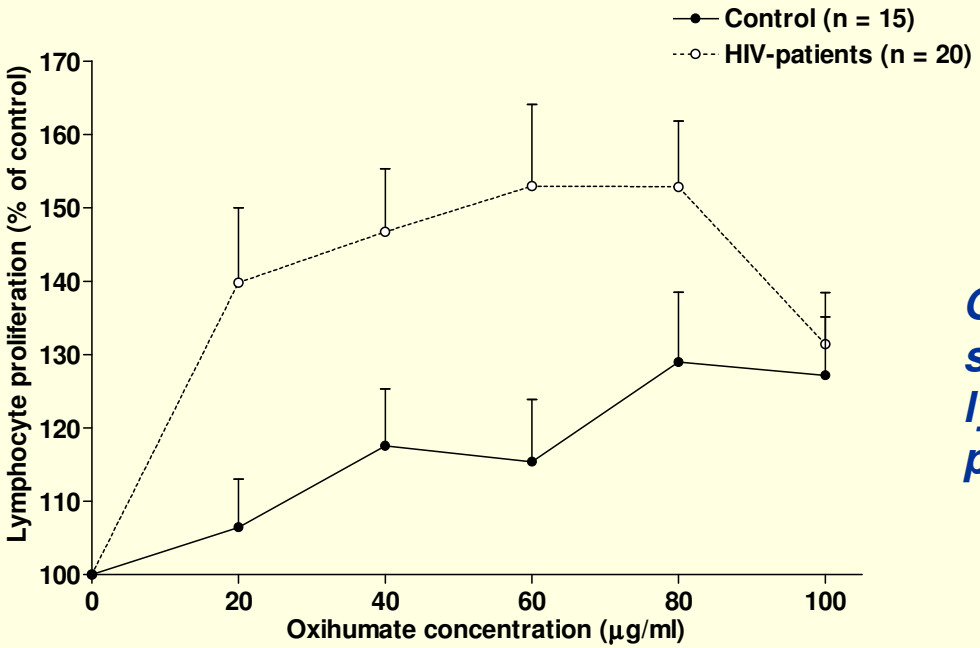
Oxihumate inhibits syncytium formation by the HIV virus when added to MT-2 cells.



Van Rensburg CEJ, Dekker J, Weis R, Smith T-L, Van Rensburg EJ, Schneider J. Investigation of the anti-HIV properties of oxihumate. Chemotherapy 2002; 48:138-143.

Oxihumate increases the production of IL2 by PHA stimulated lymphocytes obtained from normal individuals as well as HIV infected patients *in vitro.*

Effects of oxihumate on PHA stimulated lymphocyte cultures obtained from normal healthy volunteers and HIV-infected individuals



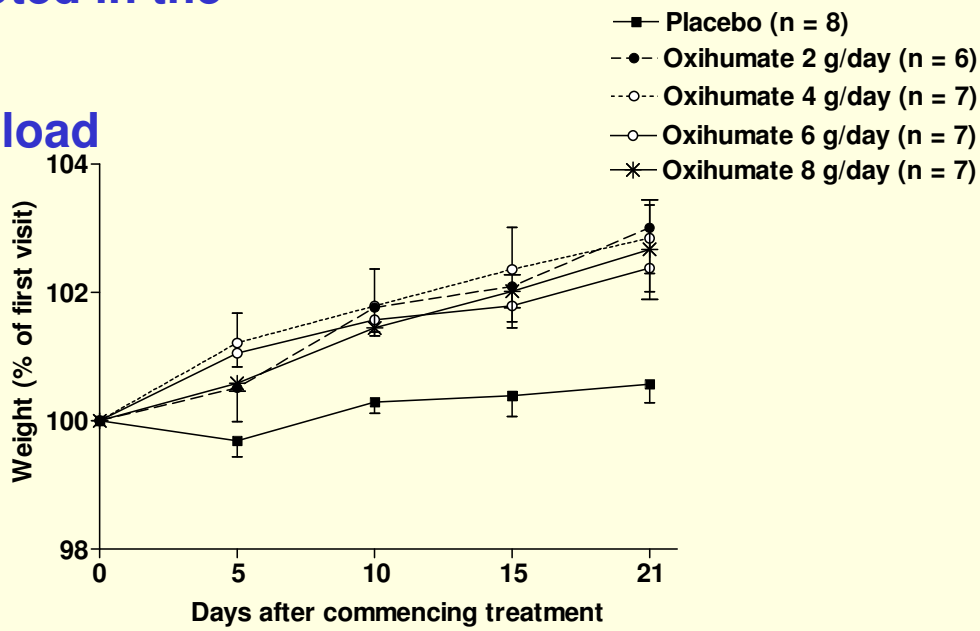
Oxihumate stimulates lymphocyte proliferation.

Jooné, G.K., Dekker, J. and van Rensburg, C.E.J. Investigation of the immunostimulatory properties of oxihumate. Z Naturfokrsch 2003; 58:263-267.

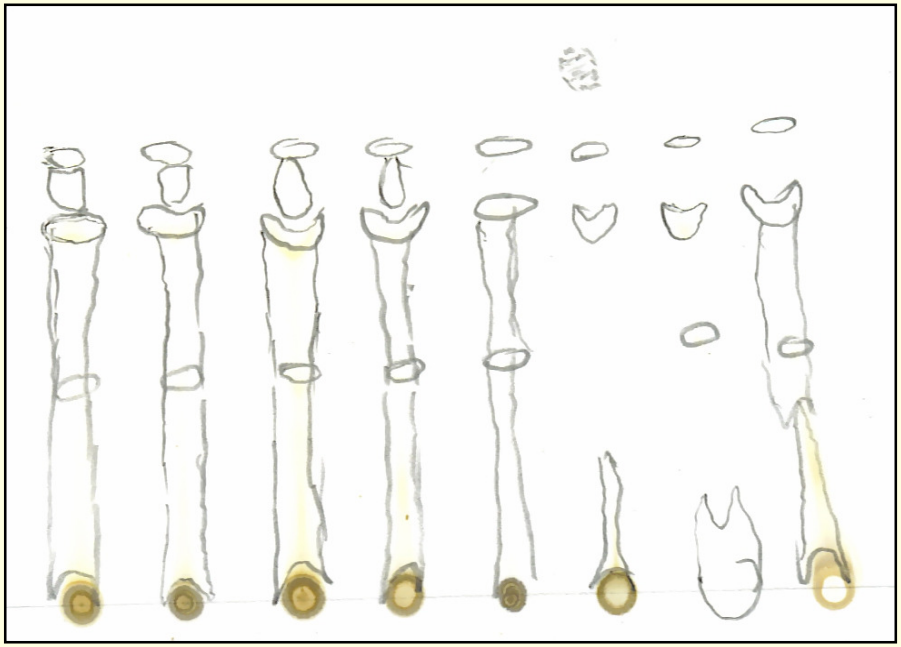
Phase I clinical trial with oxihumate in HIV infected individuals – *before the introduction of anti retroviral drugs (2002)*

5 groups: placebo, 2g, 4g, 6g, 8g oxihumate per day for 2 weeks plus one placebo group:

- **No toxicity / side effects reported in any of the 5 groups**
- **Significant increase in weight noted in the oxihumate-treated groups**
- **Oxihumate had no effect on HIV load**



Botes, M.E., Dekker, J. and van Rensburg C.E.J. Phase I trial with oral oxihumate in HIV- infected patients. DDR, 2002; 57:34-39.



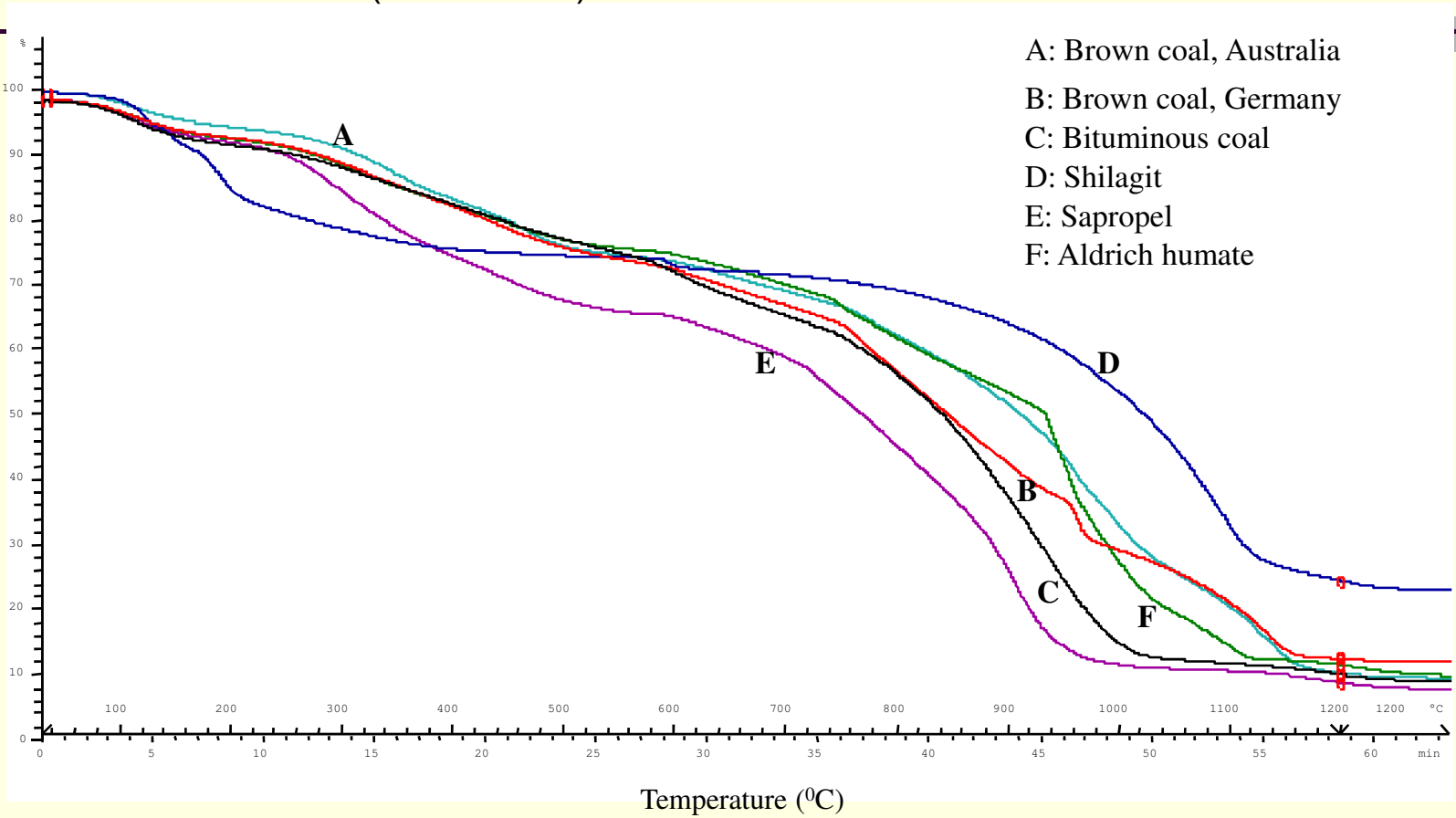
Key

1. Brown coal-Australia
2. Brown coal-China
3. Brown coal-Germany
4. Brown coal-Aldrich
5. Bituminous coal
6. Sapropel
7. Shilagit
8. Synthetic Humate

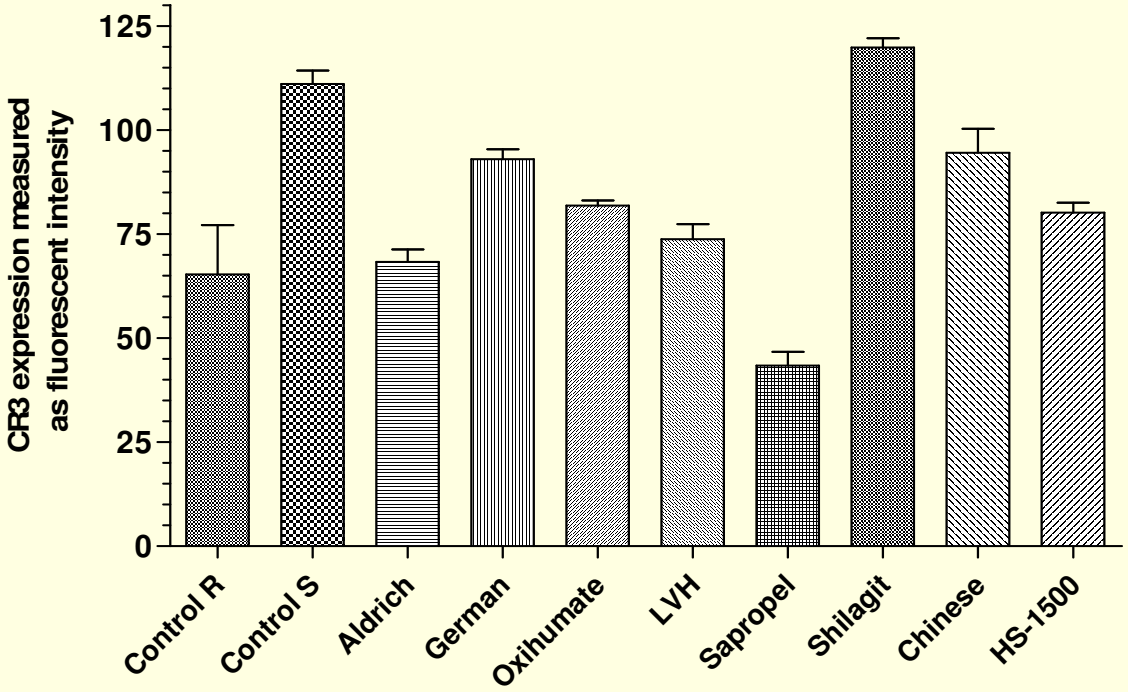
TLC Chromatogram after spotting different humic acid samples. The samples were run in Acetonitrile:Water:Ammonium hydroxide [15:8:2] mobile phase and visualized under UV light..

Thermographometric assay

(% residue)



Temperature (^{0}C)



The effect of 100µg/ml of different humic acid samples on the expression of CR3, the leukocyte adhesion molecule, on the surface of PMA-stimulated neutrophils.

Because of the variability of the results between the various potassium humate products we decided to focus on a standardized, highly soluble, product from a specific coal mine which was exceptionally pure and active.

An animal study was done to compared the effects of potasium humate, oxihumate and prednisilone on contact hypersensitivity

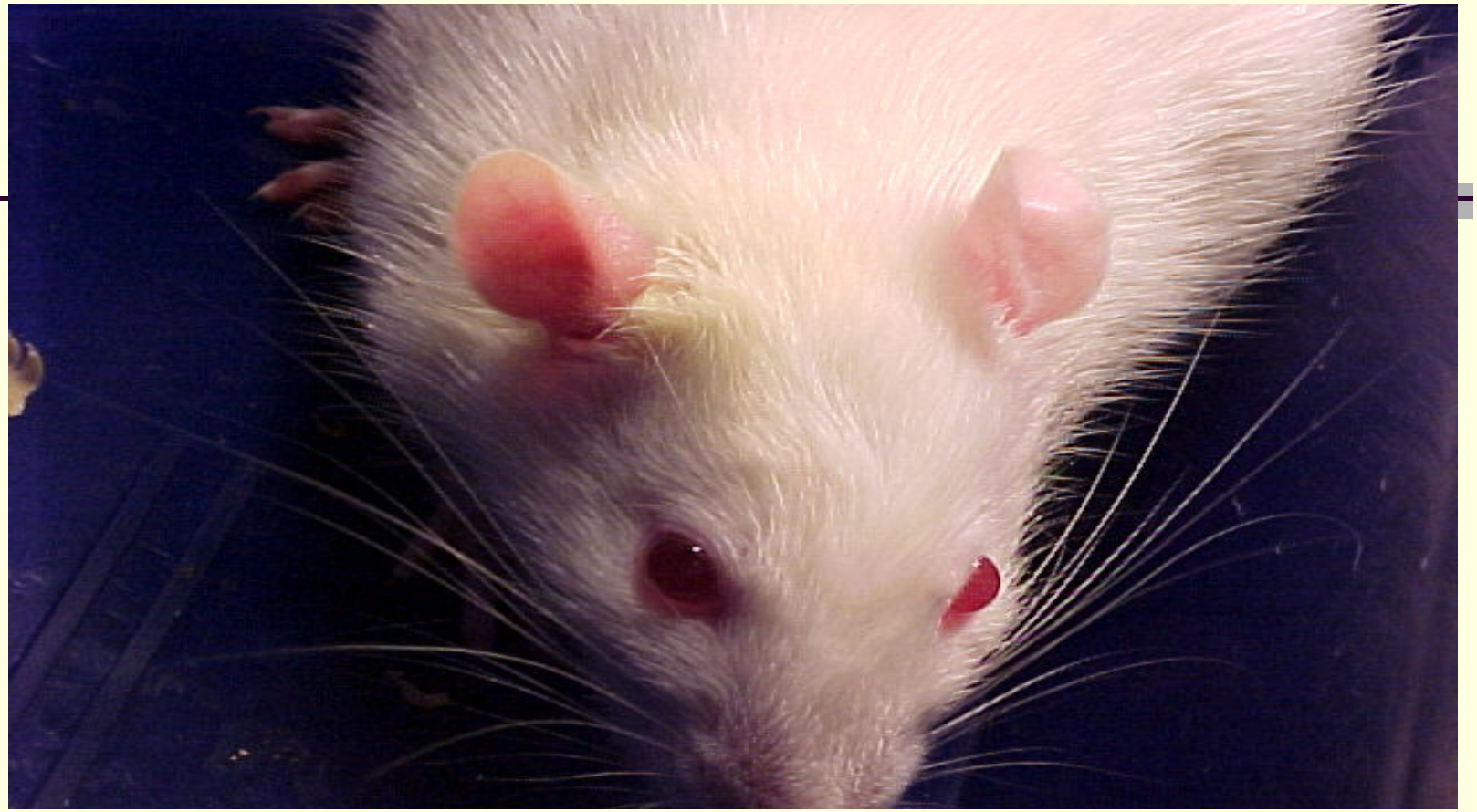
Contact hypersensitivity

Rats received by gavage: distilled water, oxihumate (61mg/kg BW) , potassium humate (61mg/kg BW) or prednisolone (one mg/kg BW) on a daily basis.

On day 0, the abdomens of the rats were painted with 2,4-dinitro-fluorobenzene (DNFB) to sensitize them.

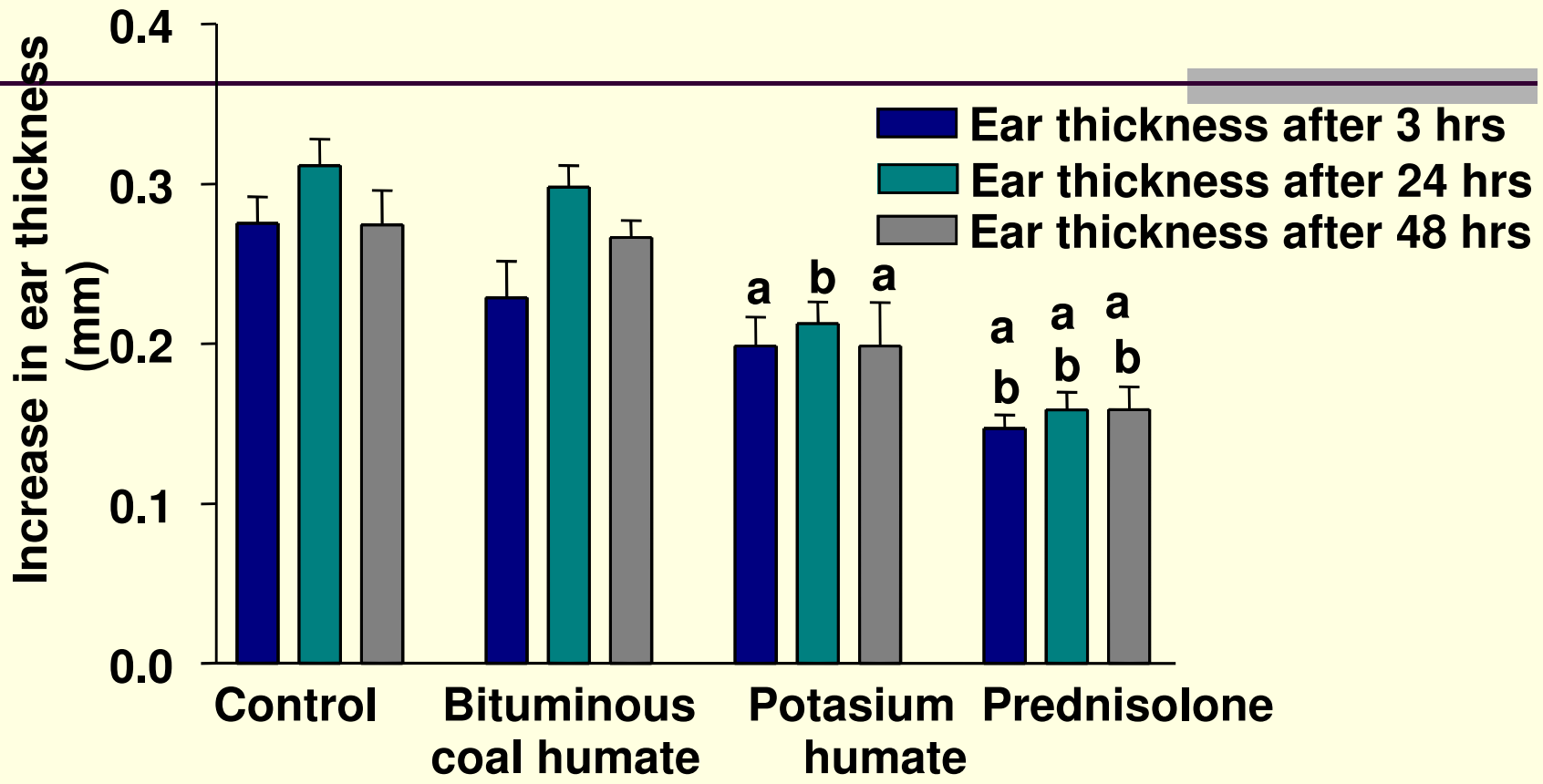
After sensitization, the rats were placed on the various treatments for 8 days.

On day 6 the rats were challenged on the right ear with DNFB. Three hours, 24h and 48h after challenge both the left (control) and right (challenged) ears were measured with an engineering caliper (Mitutoyo, Japan).



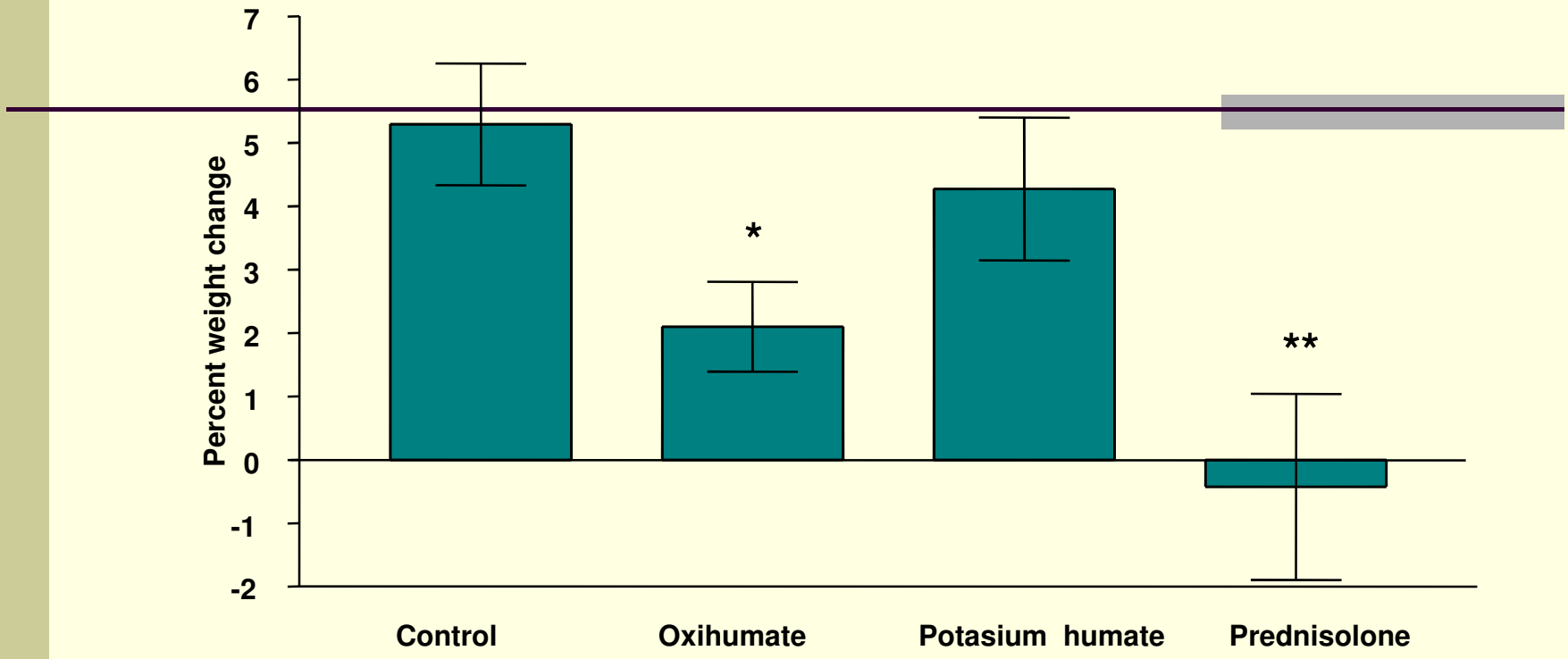
Untreated control rat demonstrating the swelling of the right ear at 24h post challenge.

Difference in ear thickness after DNFB challenge



- **Only the prednisolone and potasium humate caused a significant decrease in ear swelling at 3, 24 and 48 h after challenge**

Changes in body mass of rats after a daily treatment for one week



•No signs of toxicity were observed during the 7-day treatment period with potassium humate.

•The rats on prednisolone and oxihumate experienced a significantly slower weight gain compared to the untreated control group.

Toxicity

Rats received potassium humate dissolved in water (at 1g/kg BW) by gavage for 30 days.

Blood samples were obtained at the beginning and at the end of the study for haematological analysis.

The animals were weighed daily and monitored for signs of pain and distress.

At the end of the study, the animals were terminated and the organs studied for any abnormalities.

RESULTS

No signs of toxicity were observed.

Teratogenicity

Ten pregnant female rats received distilled water or potassium humate dissolved in water (at 1g/kg BW) by gavage from days 5 to 17 of pregnancy.

All the females as well as the pups were weighed and monitored daily.

RESULTS

No signs of toxicity were observed in the teratogenicity study.

CONCLUSION

Potassium humate inhibited the cutaneous hypersensitivity reaction in a rat model similar to prednisolone but without signs of systemic toxicity.

Van Rensburg CEJ, Snyman JR, Mokoele T and Cromarty AD. 2007. Brown coal derived humate inhibits contact hypersensitivity; an efficacy, toxicity and teragenicity study in rats. Inflammation 30 (5):148-152

In an *in vitro* mechanistic study

The effects of potassium humate were determined on

- **the release of cytokines**
- **complement activation**

Potasium humate inhibited -

the release of

TNF α
IL10
IL 1β

} associated with inflammation

in an *in vitro* culture of PHA stimulated human lymphocytes – at physiological relevant concentrations.

Joone, G.K., van Rensburg, C.E.J. An in vitro investigation of the anti-inflammatory properties of potassium humate. Inflammation 2004;28(3):169 -174.

Potasium humate inhibited

both the classical as well as alternative pathways of complement *in vitro*.

Van Rensburg, CEJ, AD Cromarty, PJW Naude. Potassium humate inhibits carrageenan induced paw oedema and a graft-vs-host reaction in rats. 2010. Inflammopharmacology 18:33-39.

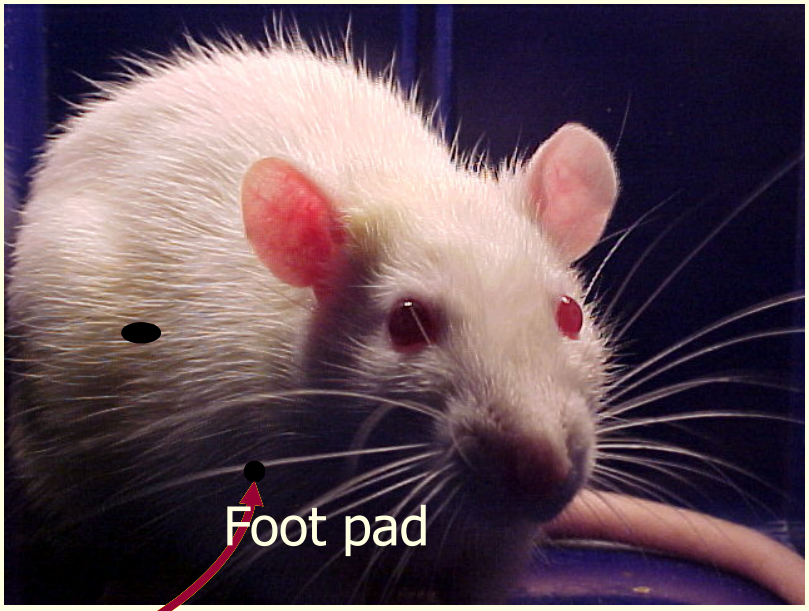
The effects of Potassium humate (at 60mg/kg) on two rat models of inflammation

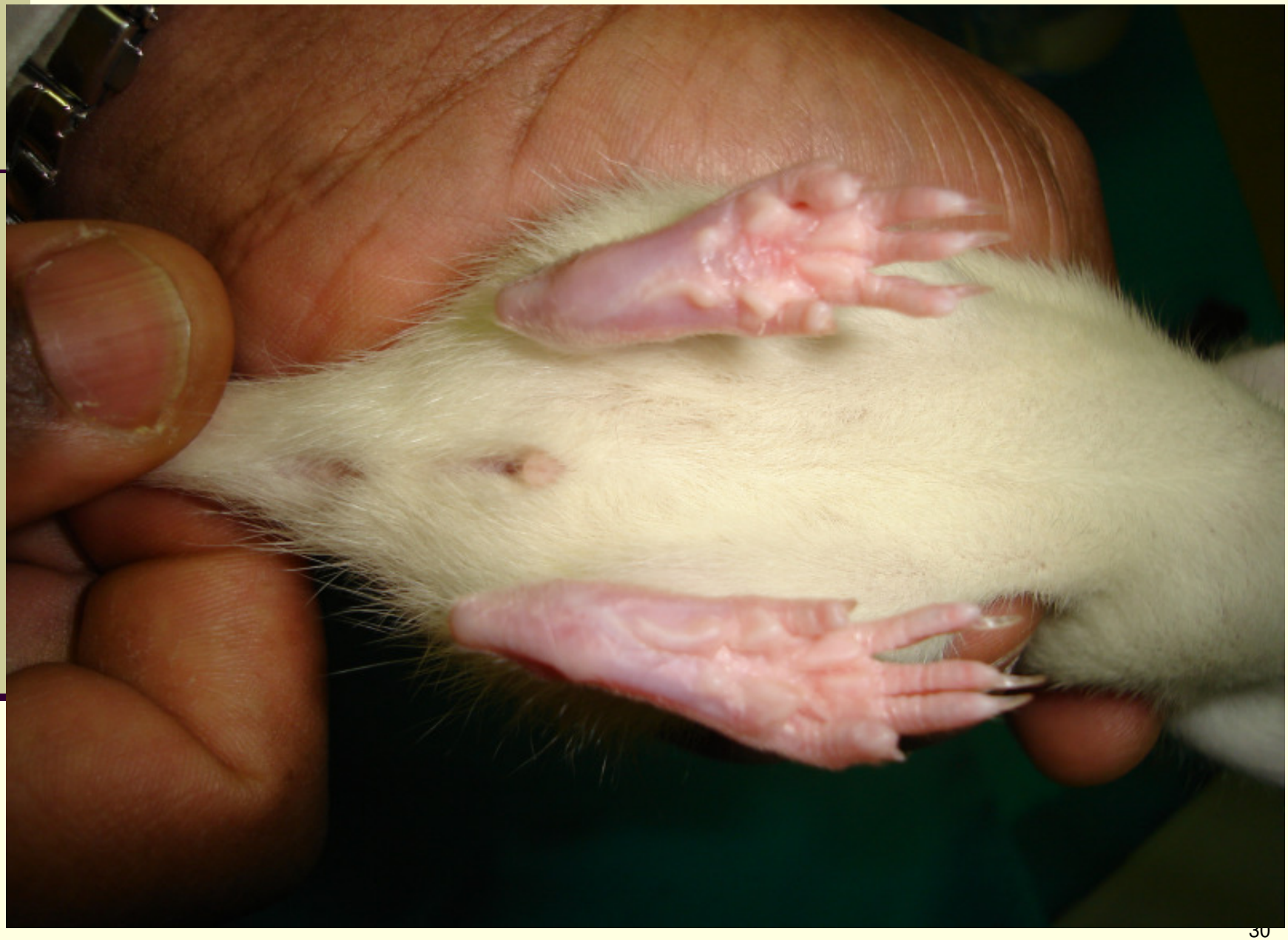
- graft vs host reaction
- carragean induced paw oedema

Graft-Versus-Host Reaction



Spleen cells






DISPOSABLE SYRINGE SET
DIGITAL PLETHYSMOMETER LE 7500
0.00



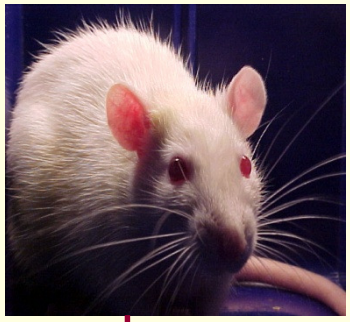
Carrageenan induced paw oedema

Control



Water day 1-5

Potassium humate



Potassium Humate day 1-5

Indomethacin

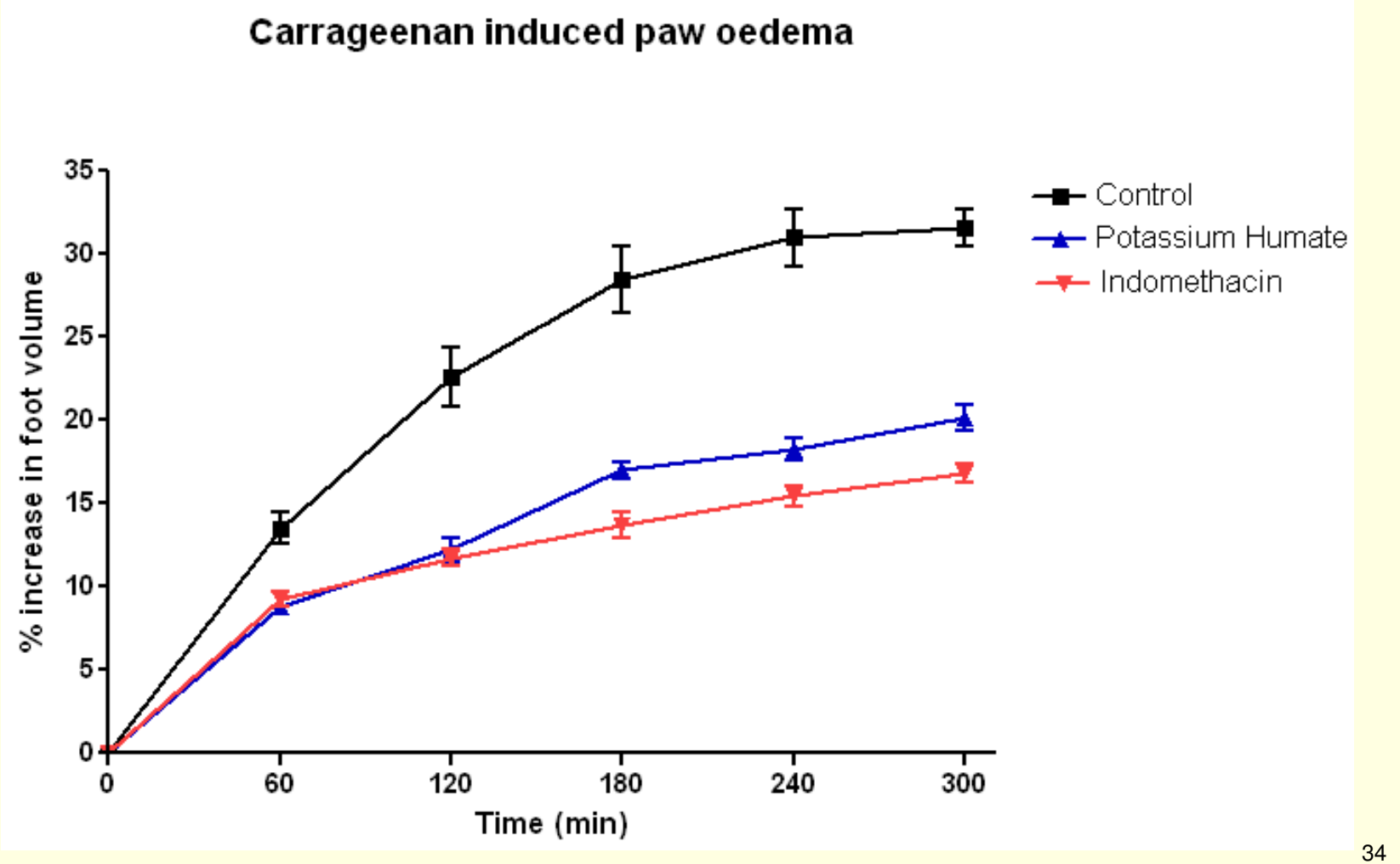


Indomethacin day Day 1-5

Carrageenan- injected in rat paw.

Swelling measure hourly

Carrageenan induced paw oedema



In conclusion:

Potassium humate at (60mg/kg body weight)

- **inhibits a graft vs host reaction**
- **inhibits carragean induced inflammation**

The antiinflammatory activity is possibly due to inhibition of complement activation and the production of inflammatory associated cytokines.

Van Rensburg, CEJ, AD Cromarty, PJW Naude. Potassium humate inhibits carrageenan induced paw oedema and a graft-vs-host reaction in rats. 2010. Inflammopharmacology 18:33-39.

First clinical trial with potasium humate:

A double blind placebo controlled study on the safety and clinical efficacy of potassium humate in the treatment of hay fever in patients with inhalant allergies.

Potasium humate was administered for one month at a dosage of 1.8g to atopic patients (n = 40) presenting with acute symptoms of hay fever.

Measurements:

- A total symptom score over a 12 hour period
- A global clinical impression was scored.
- A quality of life questionnaire.
- Measurement of the surface area of a skin prick test
- Eosinophils: A nasal swab.
- Basophils: Beckman Coulter Allergenicity Kit was used to determine activated basophils.
- Cytokines: Cytokine levels were determined by using a FlowCytomix human Th1/Th2 10plex Kit.

Results:

Total Symptom Score (TSS):

	First 48 Hours		Last 48 Hours	
	Morning	Evening	Morning	Evening
Treated	30.8	33.7	26.4 ↓	28.6 ↓
Placebo	30.1	34.5	22 ↓	24.2 ↓

	Degree of eosinophil presence in nasal smears			
	Before		After	
	Mean	SD	Mean	SD
Treated	2.63	1.12	*1.84 ↓	0.60
Placebo	2.80	0.83	2.95	0.76

Average means and standard deviations of the Th1 and Th2 cytokines before and after the trial respectively.

	Cytokine levels (pg/ml)							
Cytokines	IL-1β		IL-8		IL-4		IL-5	
	Before	After	Before	After	Before	After	Before	After
Placebo								
Average	21.93	29.77 ↑	96.66	126.23 ↑	450.94	455.98 ↑	59.79	110.97 ↑
SD	9.88	23.5	51.67	89.13	1847.11	1397.49	54.04	176.98
Treated								
Average	57.69	52.65 ↓	30.23	26.28 ↓	119.91	110.94 ↓	19.05	14.58 ↓
SD	75.94	55.65	28.47	26.62	78.65	110.98	30.76	16.57

Measurements of wheal (diameter in mm) before and after the study of the treated vs placebo groups with respect to their skin prick tests.

	Diameter of wheal (mm)			
	Before		After	
	Mean	SD	Mean	SD
Treated	8.69	4.71	*6.26 ↓	2.79
Placebo	10.66	3.85	9.67	3.91

*Indicating statistical significance ($p < 0.05$)

Conclusion

- This study confirmed that potasium possesses anti-inflammatory as well as anti-allergic properties.
- Decreased expression of IL-4, IL-5, IL-8 and IL-1β might result in decreases in recruitment of eosinophils.

Gandy JJ, JP Meeding, JR. Snyman and CEJ van Rensburg. The clinical efficacy of potassium humate in the treatment of allergic rhinitis: A double blind placebo controlled trial. 2010. Drug Development Research 71:358-363.

2nd clinical trial

A double blind placebo controlled study on the safety and clinical efficacy of potassium humate in the treatment of patients with osteoarthritis of the knee.

Introduction

- Osteoarthritis is most common form of arthritis.
- It is difficult to treat.
- All current regimes have long-term risks for patients.

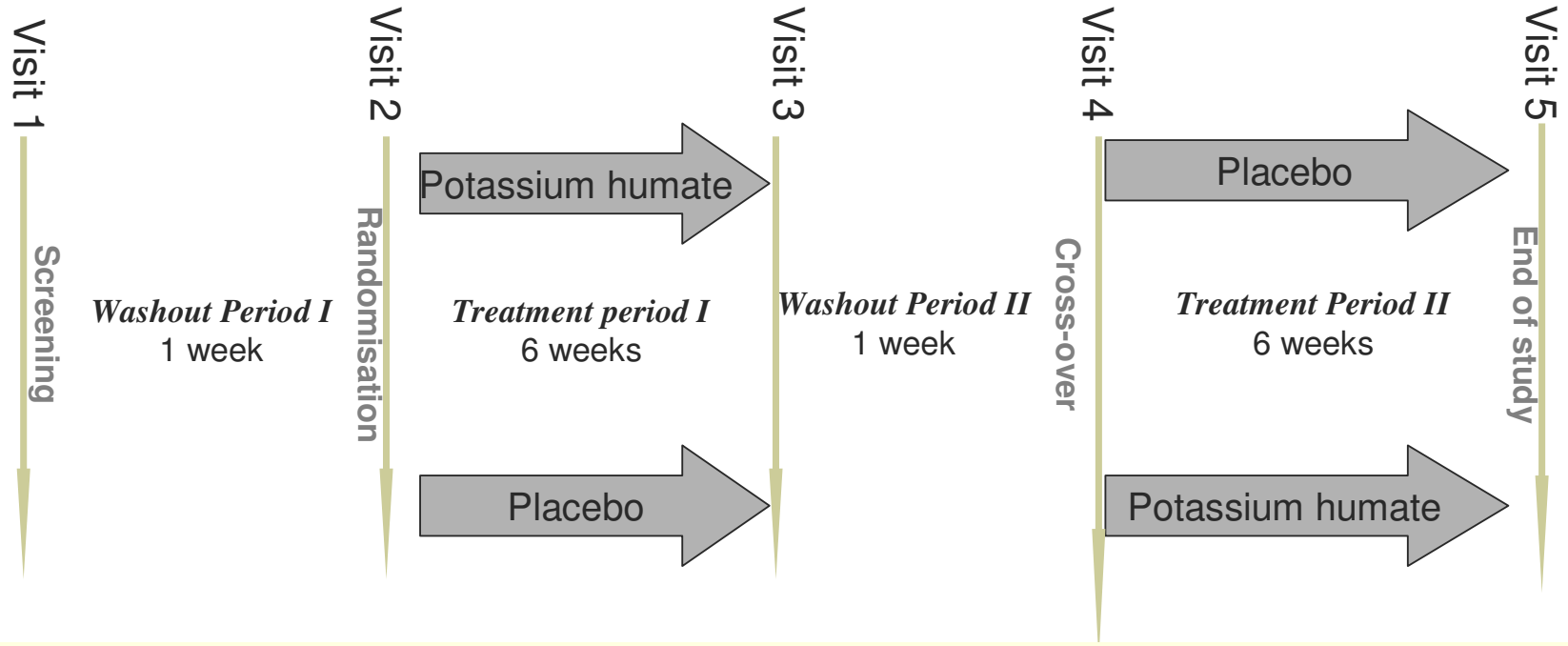
Drugs used in the past;

Associated with serious side effects

Study design:

A randomized, double-blind, placebo-controlled, single centre, cross-over, 14-week study.

Potassium humate was administered at 1.8g per day



•The secondary efficacy variables included assays for hs-CRP, rescue mediation use, adverse effects and tolerability.

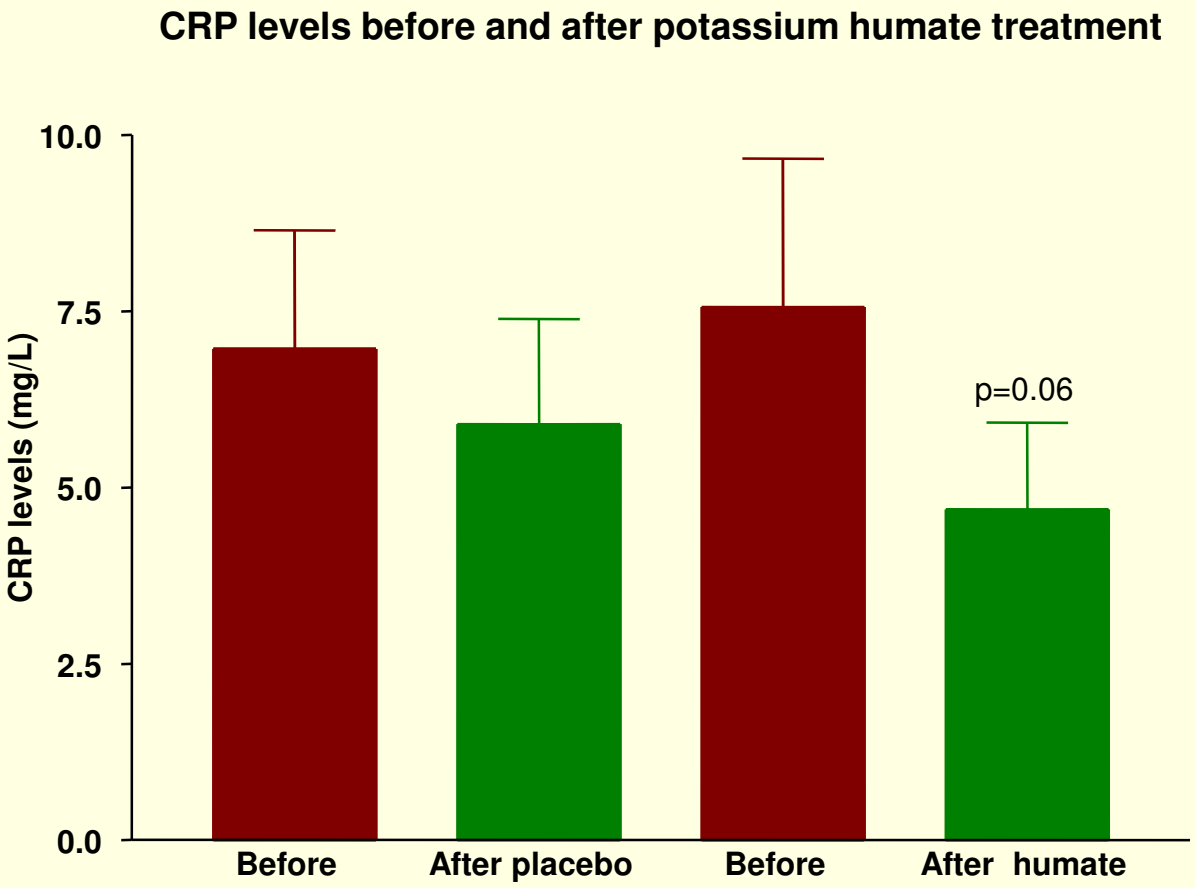
Primary outcome

A carry-over effect in the stiffness subscale was observed.

There was clinical significantly benefit in the potassium humate group over placebo (>20%) With a reduction of pain, stiffness, physical function and global well being.

Secondary outcome

•Potassium humate showed greater reduction in hs-CRP levels than placebo.



Conclusion

- Potassium humate showed benefit over placebo in patients with OA of the knee, with a reduction in hs-CRP levels and clinical benefit.
- Potassium humate had a good safety profile.

Van Rensburg CEJ, BE Badenhorst, JJ Gandy, JR Snyman. Potassium humate reduces inflammation and clincally improves the outcomes of patients with osteoarthritis of the knee. Conference Proceedings of the International Conference on Drug Discovery and Therapy. 2010. Open Conference Proceedings Journal 1:69-74.

Final Conclusion:

It has now been proven scientifically that potassium humate, obtained from a specific area:

- **is safe.**
- **possesses anti-inflammatory activity.**
- **is comparable to corticosteroids.**

Planned Future Research

To determine the safety and efficacy of potassium humate in the treatment of -

(i) rheumatoid arthritis

(ii) canine arthrits.





AcknowledgementC

- Prof Jacques Snyman
- Dr Duncan Cromarty
- Dr Gisela Jooné
- Dr Ronel Meeding

Personnel, Department of Pharmacology, UP

- Dr Elsa Badenhorst
- Mr Justin Gandy
- Mr Pieter Naudé
- Mr Tlou Mokoele

Post graduate students, Department of Pharmacology, UP

Funding was provided by :

Enerkom (Pty Ltd) [funded by the Central Energy Fund, SA]

National Research Fund [SA]

Welness SA (Natrx SA)

- Potassium humate is presently on the market for the use in inflammatory related diseases in South Africa.
- The product is receiving excellent reviews.
- The registration of this product in Canada has been formalized.

- The company will soon be seeking partners globally for distribution.

Van Rensburg C.E.J. 2015.

The anti-inflammatory properties of humic substances: A mini Review.

Phytotherapy Research, volume 29(6) : 791-795.

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Let us meet again..

We welcome you all to our future conferences of OMICS International

3rd World Congress on Pharmacology

On

August 08-10, 2016 at **Birmingham, UK**

http://pharmacology.pharmaceuticalconferences.com//