TNBS-INDUCED COLITIS IN RODENTS:

PRELIMINARY RESULTS OF A CHRONIC MODEL

Inês Silva, João Solas, Mariana Sousa, Rita Modesto, Vanessa Mateus, Rui Pinto

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SUMMARY

- Introduction
- Aim
- Materials and Methods
- Results
- Discussion
- Conclusion and Future Prospects
INTRODUCTION

INFLAMMATORY BOWEL DISEASE (IBD)

Chronic inflammatory disease of the gastrointestinal (GI) tract characterized by recurrent ulceration.¹

IBD prevalence exceeding 0.5% of the population in westernized countries.²

IBD manifests into several intestinal and extra-intestinal symptoms, mainly related to inflammation.³

INTRODUCTION

IBD includes **Crohn’s disease** (CD) and **Ulcerative colitis** (UC)


TREATMENT OF IBD

- Induce and maintain the patient in remission
- However do not modify or reverse the underlying pathogenic mechanism

Nonclinical studies for emerging therapeutic strategies

Adaptado de Katzung & Trevor's Pharmacology: Examination & Board Review, 10.
# INTRODUCTION

## ANIMAL MODELS

<table>
<thead>
<tr>
<th>MODEL</th>
<th>SPECIES</th>
<th>METHOD OF INDUCTION</th>
<th>TIME COURSE</th>
<th>DISEASE LOCATION</th>
<th>TYPE OF COLITIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNBS</td>
<td>Rats, mice and rabbits</td>
<td>TNBS enema (20-30mg in 30-50% EtOH)</td>
<td>3 days – 8 weeks</td>
<td>Small intestine or colon</td>
<td>Acute and chronic</td>
</tr>
<tr>
<td>DSS</td>
<td>Hamsters, mice and rats</td>
<td>2 - 10% DSS feeding</td>
<td>5 days – 15 weeks/</td>
<td>Colon</td>
<td>Acute and chronic</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>Rats</td>
<td>1 – 10% acetic acid enema</td>
<td>1 day – 3 weeks</td>
<td>Colon</td>
<td>Acute</td>
</tr>
<tr>
<td>Carrageenan</td>
<td>Rats, guinea, pigs and rabbits</td>
<td>Variable oral dosing</td>
<td>1 – 4 weeks</td>
<td>Cecum and colon</td>
<td>Acute and chronic</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Rats</td>
<td>Oral or SC once or twice</td>
<td>&lt; 1 - 8 days</td>
<td>Small intestine</td>
<td>Acute</td>
</tr>
<tr>
<td>Oxazalone</td>
<td>Mice and rats</td>
<td>Intracolonic</td>
<td>Rapid</td>
<td>Colon</td>
<td>Acute</td>
</tr>
</tbody>
</table>

I. CHEMICALLY INDUCED MODELS
**INTRODUCTION**

**ETHANOL** is proposed to elicit a transient increase in intestinal permeability.\(^5\)

**TNBS** reaches the subepithelial space and haptenate tissue and microbial proteins.\(^6\)

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Aim

Evaluate the efficacy of new drugs in Inflammatory Bowel Disease through an animal model of TNBS-induced chronic colitis
MATERIALS AND METHODS

ANIMALS

Male CD-1 mice, 30-40g in weight and 6-10 weeks of age, were housed in standard polypropylene cages with *ad libitum* access to food and water in the Faculty of Pharmacy Central Animal Facility in the University of Lisbon.
MATERIALS AND METHODS

TNBS-INDUCED COLITIS

- Mice were left unfed during 24h
- Mice were anesthetized with Ketamine + Xilazine IP
- 100µl of TNBS (in 50% ethanol) was administered through a catheter inserted into the rectum
- Mice were kept for 1 min in a Trendelenburg position to avoid reflux
**TNBS Scheme Administration**

- **Day 0**: TNBS 1%
- **Day 1**: NaCl 0.9%
- **Day 2**: Ethanol 50%
- **Day 3** to **Day 4**: 6 weeks
- **Day 5** to **Day 6**: 6 weeks
- **Day 7**: Euthanasia
RESULTS

CLINICAL SIGNS AND SYMPTOMS

SURVIVAL

Edema of the anus
Soft stools
Morbidity
RESULTS

BIOCHEMICAL MARKER

Fecal Hemoglobin

Legend: *** p<0.0001
RESULTS

BIOCHEMICAL MARKER

TNF-ALPHA

Legend: *** p<0.0001
RESULTS

**BIOCHEMICAL MARKER**

**IL-10**

![Graph showing IL-10 levels across different conditions.

Legend: ** p<0.01; *** p<0.0001

Legend: ** p<0.01; *** p<0.0001
RESULTS

**Biochemical Marker**

**ALP**

Legend: *** p<0.0001
RESULTS

RENAL MARKERS

UREA

CREATININE

Legend: * p<0.05; ** p<0.01
RESULTS

HEPATIC MARKER

ALT

Legend: * p<0.05; *** p<0.0001
CONCLUSION

These findings seem to propose

4 administrations 1% TNBS for the induction of chronic colitis
THANK YOU!

Acknowledgments:

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