



MITIGATION OF GASTRIC ULCERS AND PROTECTION AGAINST NSAID-INDUCED DAMAGE BY MANNANPRO®, AN ALOE-DERIVED POLYSACCHARIDE

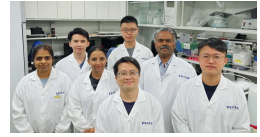


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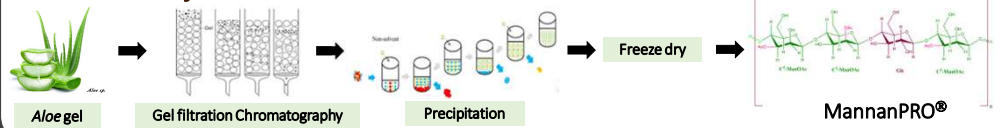
ABSTRACT

The gastroprotective efficacy of *Aloe*-derived polysaccharide MannanPRO® was studied in rat gastric mucosa cells (RGM1) and Sprague-Dawley rats. MannanPRO® significantly promoted gastric mucosa re-epithelization, increased gastric pH, and reduced total gastric acidity in experimental rats. This observation also correlated well with results obtained from cell-based assays, imaging, and molecular analyses. MannanPRO® functions as a protective shield against cellular stresses caused by inflammatory gut disorders and augments cellular repair mechanisms toward maintaining healthy mucosa barrier function.

INTRODUCTION

- Non-steroidal anti-inflammatory drugs (NSAIDs) are considered to be one of the most important causative factors for gastric damage. Indomethacin suppresses the cell survival mechanism by early depletion of mucosal prostaglandins E2 (PGE2) which is important for regulation of immune responses, and gastrointestinal integrity.
- MannanPRO® isolated from *Aloe barbadensis* L. leaves possesses immunoregulation, anti-cancer, anti-oxidation, wound healing, bone proliferation promotion, neuroprotection, and intestinal health promotion activities.

Production of MannanPRO®



OBJECTIVES

To evaluate the gastroprotective effect of MannanPRO® on the damaged gastric mucosa of Sprague-Dawley rats caused by over-accumulation of gastric juice

Cytotoxicity study of MannanPRO® in RGM1 cell line

Mitigation of NSAID (indomethacin)-induced cellular damage by MannanPRO®

METHODOLOGY

Oral administration of MannanPRO®

Low dose: 0.55 mg/kg/day
Medium dose: 1.67 mg/kg/day
High dose: 2.78 mg/kg/day



In vivo
Pylorus ligation
Accumulation of gastric juice for 4 h
(Ulcer formation)

- ◆ Gastric pH
- ◆ Total gastric acidity
- ◆ Gastric damaged area
- ◆ Gastric lesion index



MannanPRO®
NSAID (Indomethacin)

In vitro



- ◆ Cell viability
- ◆ Cell count
- ◆ Cell cycle
- ◆ LDH leakage
- ◆ ROS detection

RESULTS

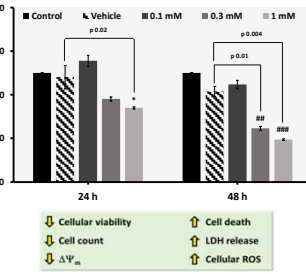
MannanPRO® Efficacy Evaluation and Observation

- Clinical: abnormal behavior or clinical symptoms or death
- Physiological: body weight, food, and water intake
- Gastroprotective effect: Shay's Ulcer method

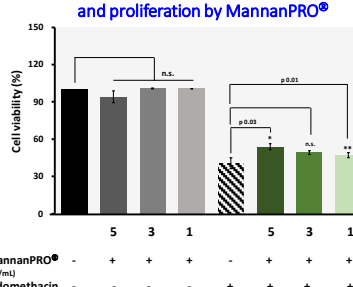
Gastric pH		Gastric Damaged Area	
Nomenclature	pH level	Nomenclature	Gastric damaged Area (mm ²)
Water only	1.46	Water only	0.75
Positive control (5-ASA)	2.12	Positive control (5-ASA)	0.4 (# 1.8 fold)
Low	2.10	MannanPRO® Low	0.34 (# 2.2 fold)
Medium	1.7	Medium	0.29 (# 2.2 fold)
High	2.58 (# 1.7 fold)	High	0.34 (# 2.2 fold)

Total gastric acidity		Gastric Lesion Index	
Nomenclature	Total acidity (mEq/L)	Nomenclature	Gastric lesion index
Water only	56.89	Water only	8.32
Positive control (5-ASA)	18.83 (# 3 fold)	Positive control (5-ASA)	4.54 (# 1.8 fold)
Low	35.78 (# 1.6 fold) (# 1.9 fold)	Low	4 (# 2.1 fold)
Medium	33.97 (# 1.6 fold) (# 1.8 fold)	Medium	3.5 (# 2.3 fold)
High	30.97 (# 1.8 fold) (# 1.8 fold)	High	4.02 (# 2.1 fold)

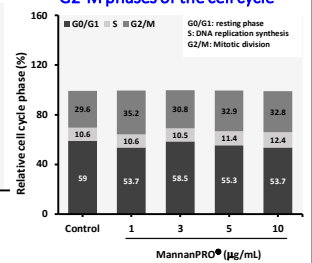
Mucosa damage by Indomethacin



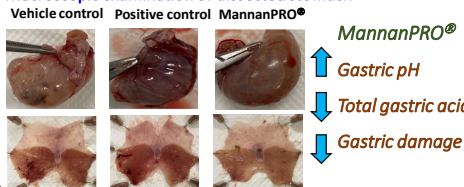
Repair, re-epithelization, and proliferation by MannanPRO®



MannanPRO® increases S and G2-M phases of the cell cycle

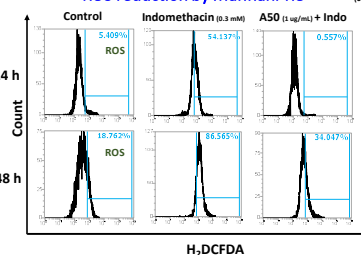


Macroscopic examination of dissected stomach

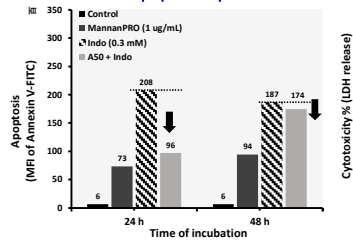


MannanPRO®
↑ Gastric pH
↓ Total gastric acidity^{48h}
↓ Gastric damage

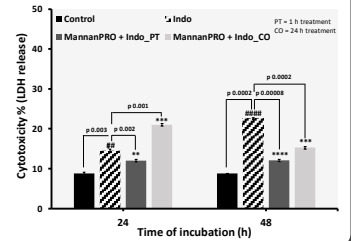
ROS reduction by MannanPRO®



Reduction in apoptosis by MannanPRO®



Reduced LDH release by MannanPRO®



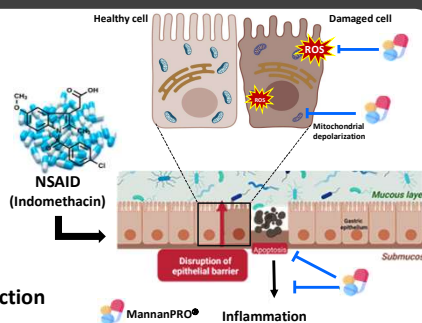
CONCLUSION

Pylorus ligation

- Gastric damage
- Ulceration
- Inflammation
- Mucosal erosions
- Hemorrhage

MannanPRO® Healed and healthy gut mucosa

- ↓ Gastric acidity
- ↓ Ulcers
- ↓ Gastric damage
- ↓ Oxidative stress
- ↑ Cell viability
- ↑ Cell proliferation
- ↑ Mitochondrial function



ACKNOWLEDGMENT

The authors thank Chen-Yin Fie and Wei-Shiun Huang, Dazzeon Biotechnology Co. Ltd., Taiwan for their useful suggestions in conducting animal studies. Authors also grateful to Dr. Jang-Shun Wang, University of Kang Ning for sharing his expert opinions and suggestions related to *In vitro* studies.

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NSAIDs

