

## Introduction



Figure 1: severe oral ulcerations that are painful and affect oral functions

Oral mucositis presents itself as severe mouth sores, oral and gastrointestinal ulcers, difficulty swallowing, and redness of the mouth as a result of cancer treatment with head and neck cancer. Oral mucositis can disrupt patient treatment. This debilitating side effect affects approximately 500,000 patients undergoing cancer therapy in the U.S.

Mucositis follows a five step model that involves the stages of initiation, upregulation, signaling and amplification, ulceration and healing. Oral mucositis begins with an innate immune response which is triggered by a family of Pattern Recognition Receptors (PRRs). There are four classes of PRRs and the upregulation of certain PRRs can lead to the prevention of the initiation phase of mucositis<sup>4</sup>.

With cancer being the leading cause of death in the U.S. and many patients fall victim to oral mucositis as an adverse side effect, it is important to find a way to prevent the development of oral mucositis.

## Traditional Treatment Methods and Disadvantages

Treatment	Disadvantage(s)
Cryotherapy <sup>1</sup>	Development is not prevented
Mouthwashes and Rinses <sup>1</sup>	Development not prevented, pain reduced slightly
Antibiotics: Polymyxin E tobramycin and amphotericin B <sup>2</sup>	Increase risk of toxicity and resistance to antibiotics
Accelerated radiotherapy <sup>2</sup>	Development of influenza. Low tolerance for treatment. Persistence of severe oral mucositis
Morning radiotherapy <sup>2</sup>	Toxicity rate not reduced
Povidone iodine <sup>2</sup>	Patients do not like the taste

Table 1. Disadvantages of current treatments for oral mucositis.

## Receptors of Inflammation in Human Body

### Pattern Recognition Receptors for Oral Mucositis

Pathogen Associated Molecular Patterns (PAMPs)	Damage Associated Molecular Patterns (DAMPs)
<ul style="list-style-type: none"> <li>Membrane bound</li> <li>Toll-Like Receptors (TLRs)</li> <li>C-Type Lectin Receptors (CLRs)</li> </ul>	<ul style="list-style-type: none"> <li>In cytoplasm</li> <li>NOD-Like Receptors (NLRs)</li> <li>RIG-Like Receptors (RLRs)</li> </ul>

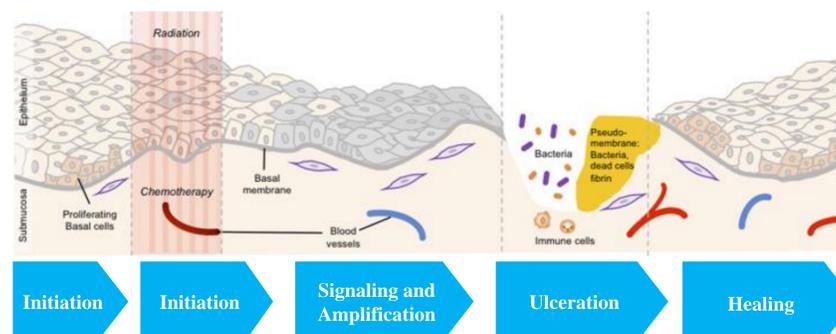
Table 2. Breakdown of Pattern Recognition Receptors (PRRs)

Pattern recognition receptors (PRRs) are divided into pathogen associated molecular patterns (PAMPs) and damage associated molecular patterns (DAMPs).

PAMPs are membrane bound receptors and DAMPs are in the cytoplasm

TLRs and NLRs may play a role in the innate regulation of oral mucositis

## Mechanism of Inflammation



Five Steps Progression of Oral Mucositis<sup>6</sup>

Initiation	Upregulation	Signaling and Amplification	Ulceration	Healing
<ul style="list-style-type: none"> <li>Damage in DNA strand</li> </ul>	<ul style="list-style-type: none"> <li>Activation of transcription factors</li> <li>Increase in inflammatory cytokines production</li> </ul>	<ul style="list-style-type: none"> <li>Activation of ceramide and caspase pathways</li> </ul>	<ul style="list-style-type: none"> <li>Breach in mucosal barrier</li> <li>Occurrence of bacterial and fungal infections</li> </ul>	<ul style="list-style-type: none"> <li>Normalization of the oral microbial environment</li> <li>Regeneration of cells</li> </ul>

Table 3. Model for oral mucositis

## New Treatment Approaches

Name	Contents	Formulation	Outcome
MuGard	Glycerin, benzyl alcohol, sodium saccharin, carbomer homopolymer A, potassium hydroxide, citric acid, polysorbate 60, phosphoric acid	Mucoadhesive gel topical agent	Reduction in severity and development of mucositis and pain
Glutamine	Glutamine amino acid	Anti-inflammatory agent	Reduction in occurrence, severity and duration of mucositis,
N-acetyl cysteine		Antioxidant	Decrease in severity in extreme mucositis

Table 4. Approaches to treatment of oral mucositis<sup>5</sup>

## Natural Methods of Formulation (7)

Natural Ingredient	Type of Use	Polymer	Nanomaterial Formation
Coffee plus honey	Topical and swallow	No polymer	The best reduction in severity was achieved in coffee plus honey group.
Peppermint	Topical (mouthwash)	No Polymer	Significant reduction in frequency of mucositis
Olive leaf extract	Topical (mouthwash)	No Polymer	Significant reduction in frequency of mucositis
Curcuma longa	Mouthwash and as nano-formulation	Eudragit and Pluronic F68	Future experimentation needed
Resvaterol	Mouthwash and as nano-formulation	Eudragit and Pluronic F69	Future experimentation needed
Quercetin	Mouthwash and as nano-formulation	Eudragit and Pluronic F70	Future experimentation needed

Table 5. Use, polymer, and nanomaterials for natural methods

## Summary

In summary, oral mucositis is a clinically important, deleterious consequence of chemo and radiotherapy, for which no effective treatment has been found to date.

Mucositis lesions can be painful, affect nutrition and quality of life, and have a significant economic impact.

This review discusses current clinical practices in the management of oral mucositis and emphasizes that new approaches need to discover new formulations.

## References and Acknowledgements

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