

THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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Guest Author:
Sydney Lee, 4th Year
Student Pharmacist,
University of
Pittsburgh School of
Pharmacy

**Palliative Care
Pharmacy Team:**

**Clinical Pharmacy
Specialist:**

**Maria Felton Lowry,
PharmD, BCPS, BCGP**
Assistant Professor
University of Pittsburgh
School of Pharmacy,
Department of Pharmacy
and Therapeutics
Palliative
Care Clinical Pharmacy
Specialist
UPMC Palliative and
Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you
would like the pharmacy
team to answer, please
send your suggestions to:
lowrymf@upmc.edu

TODAY'S TOPIC: Honey for Oral Mucositis

Background:

Oral mucositis is a highly painful adverse effect of some chemotherapies and radiation used to treat cancer. Patients develop painful sores in the mouth, leading to infections, change in taste, weight loss, and reduction in quality of life. This effect can be dose limiting or lead to delays in care and is associated with higher mortality. The Multinational Association of Supportive Care in Cancer and International Society of Oral Oncology (MASCC/ISOO) have published guidelines for the management of oral mucositis, naming several treatments including cryotherapy, zinc supplementation, and honey. There are very few treatments available for mucositis, and very little efficacy data all around. Some of the literature for the use of honey is conflicting.

So, what do we know about honey for mucositis?

Safety:

- Generally safe and well tolerated for those >1 year of age (infants do not have protections against the traces of botulinum toxin that may appear in honey and can become ill or die)
- Some patients report topical irritation where it is used, or mild gastrointestinal symptoms like nausea and stomach aches when consumed.
- Patients with diabetes/pre-diabetes may have an increase in blood sugar - while manuka honey may have a lower glycemic index, it is composed of carbohydrates.
- Limited/conflicting evidence of possible drug interactions: increase in phenytoin levels or bleeding risk, though evidence is derived from in vitro and animal research.
- Mixed evidence of CYP3A4 enzyme induction in humans using honey products, but this is likely not clinically significant.

Tolerability:

While many patients do not have issues tolerating honey products, some medicinal honeys have a bitter taste. In some trials, patients ate honey as-is, while others mixed it into an oral rinse.

Efficacy:

There is some evidence for the use of honey, though much of it is mixed. There are numerous types of honey, coming from different bees and flower types.

Pure Honey:

[Support Care Cancer. 2003 Apr;11\(4\):242-8.](#)

- 40 patients received radiation \pm 20 mL of pure honey 15 minutes before and after, and 6 hours after radiation
- Honey group had significantly lower rates of grade 3-4 mucositis (20% vs. 75%, $p = <0.001$)
 - per Radiation Therapy Oncology Group (RTOG) as confluent mucositis, where patients may cough up blood or have spontaneous hemorrhage/necrosis
- Both groups had comparable rates of overall mucositis, and mean onset/duration of mucositis were not significant, but more patients had stable/increase in body weight ($p = 0.05$), and fewer interrupted treatment days ($p = <0.05$).
- Newer studies have not affirmed results of this magnitude.

[Clin Oral Investig. 2019 Apr;23\(4\):1811-1821.](#)

- Single-blind RCT (n=53) acute myeloid leukemia patients received honey mouthwash (n = 17), oral care (n = 17), or control treatment (n = 19)
- Assessed weekly, and their mucositis was graded using WHO criteria: Grade 0 ulcer free, Grade 1 redness/pain, Grade 2 redness/ ulceration, Grade 3 severe redness/ulceration, Grade 4 profound ulceration that cannot be easily repaired.
- No differences in the first two weeks, in the third and fourth weeks, the difference in the honey and oral care groups when compared to placebo significantly favored honey ($p <0.01$).
- Honey group patient body weight increased by 3.72%, while decreasing in the other groups, and the difference was statistically significant ($p <0.01$)

Manuka honey, hailed for antimicrobial properties from methylglyoxal, appears to be a popular choice in research. It is made in New Zealand, using nectar from a Manuka bush:

[J Pediatr Nurs. 2023 May-Jun;70:e48-e53.](#)

- Single-blind RCT of 42 pediatric patients with leukemia receiving manuka honey (n = 17), olive oil (n = 15), or control (n = 14)
- Manuka honey alone offered statistically significant improvements in healing compared to the control group based on WHO classifications (mean 1.00 ± 0.63 vs. mean 2.50 ± 0.71), and significant pain reduction affirming the effectiveness of manuka honey for mucositis.

[Br J Oral Maxillofac Surg. 2012 Apr;50\(3\):221-6](#)

- However, a double-blind RCT of manuka honey vs. golden syrup found for 131 patients, there was no significant difference in rates of Grade 3-4 mucositis, colonization, weight loss, need for tube feeding, or duration of opioid analgesia.

[Support Care Cancer. 2014 Mar;22\(3\):751-61](#)

- Another double-blind RCT of 106 patients comparing manuka honey with placebo found no significant difference in rates of Grade 3 mucositis (RTOC criteria). This study had high dropout rates due to nausea and missing data.

Price:

- Numerous honey formulations are available on the market, at a variety of price points: \$20-\$200, depending on quantity, brand, and ratings.
- While there is no US certification, manuka honey products from New Zealand have robust labeling standards. Also, some products have Unique Manuka Factor (UMF) certification, determined by a business organization requiring independent testing for purity, quality, freshness, and authenticity, where higher ratings mean increased potency, though the clinical significance of potency is unclear.

Simplicity:

There are no current guidelines recommendations for using honey products, and it would be reasonable to either eat the honey as is or to dissolve it into a rinse based on preference and convenience. There are also no robust recommendations for dosages or timing, but based on the trial evidence, 15-20 mL (~ 1 tablespoon) once or twice per day could be effective.

Sydney's thoughts:

- There is some research to suggest that honey may be an effective treatment for patients with chemotherapy or radiation induced mucositis, though evidence is mixed.
- Honey is likely safe in patients over 1 year old, though there are possible minor/theoretical drug interactions and risk of hyperglycemia in patients with diabetes.
- Honey is commercially available in numerous formulations. Cost is variable.

CLINICAL PEARL: If patients >1 year old are experiencing mucositis, trying 15-20 mL (~1 tablespoon) of honey either by itself or dissolved into water to make a rinse taken once or twice daily may provide some benefit, with minimal risk.

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