NUTRITION

Sugar content, cariogenicity, and dental concerns with commonly used medications

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Because of the bitter taste of many medications, sugar (sucrose) is often combined with other ingredients to provide more palatable forms that may improve patient compliance.[1-3] Sucrose provides other functional properties in addition to sweetness; it also acts indirectly as a solvent, demulcent, and bulking agent.[4] Unfortunately, the biofilm covering teeth (plaque) contains over 500 species of bacteria that consume carbohydrates such as sucrose, creating acid as a by-product. If there is ongoing exposure to sucrose, an acidic environment is created that can decalcify tooth enamel, leading to carious lesions. Left untreated, caries can lead to pulp infection and potential tooth loss; hence, alternative sweeteners such as sorbitol and xylitol are increasingly common in medicinal preparations in lieu of sucrose.[5,6]

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ABSTRACT

Background and Overview. Oral adverse events such as cariogenicity are often overlooked as drug-associated effects because the sugar content of many medications may be negligible compared with the patients' overall dietary intake of sugar. There are, however, several liquid formulations of medications with significantly high sugar content that are commonly used in patients with swallowing difficulties. These medications may be associated with negative oral health sequelae and should be considered part of the oral health care providers' differential diagnosis of oral pathologies.

Methods. We reviewed the literature regarding the sugar content of oral liquid medications commonly prescribed by oral health care providers, with consideration to their caries potential. Where not available via public sources, pharmaceutical companies were contacted directly for additional information on the sugar (carbohydrate) content of these oral liquid medication formulations.

Results. Over 50 commonly used oral liquid medications prescribed for patients with swallowing difficulties were reviewed and found to contain sugar in varying amounts up to 4 grams per dose (usually 1 teaspoon or 5 milliliters). Patients who are required to take multiple doses per day of these sugar-containing oral liquid medications may be at increased risk for caries and associated oral health consequences.

Conclusions and Practical Implications. Recognition and avoidance of sugar-containing oral liquid medications can help clinicians optimize patient treatment, decreasing the risk for potential drug-induced caries while emphasizing patient safety and improved oral health.

Key Words. Drugs; dental care; cariogenicity; patient safety; sugar content.
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TABLE 1

Sugar-containing oral liquid medications commonly prescribed by oral health care providers.[11-15]

MEDICATION	ACTIVE INGREDIENT CONCENTRATION AVAILABLE, mg*/5 mL†	USUAL ADULT DOSE	SUCROSE CONTENT, g‡/5 mL
Antibiotics			
Amoxicillin	125, 200, 250, 400	250-500 mg every 8 h	1.70, 1.68, 1.85, 1.88
Amoxicillin–clavulanic acid	125-31.25, 250-62.5	250-500 mg every 8 h or 875 mg every 12 h	0.53, 0.67
Azithromycin	100, 200	250-500 mg once daily	3.86, 3.87
Bactrim	200-40	4 mL every 12 h	3.2
Cefaclor§	125, 250, 375	250-500 mg every 8 h	2.3, 2.1, 2.0
Cefadroxil§	250, 500	500-1,000 mg every 12 h	2.2, 1.9
Cefdinir	125, 250	300 mg every 12 h	2.9, 2.7
Cefpodoxime§	50, 100	100-400 mg every 12 h	3.0, 3.1
Cefprozil§	125, 250	500 mg every 12-24 h	2.2, 2.0
Cefuroxime§	125, 250	125-500 mg every 12 h	3.2, 2.4
Cephalexin	125, 250	250-1,000 mg every 6-12 h	3.0, 3.0
Ciprofloxacin§	250, 500	250-750 mg every 12 h	1.4, 1.3
Clarithromycin§	125, 250	250-500 mg every 12 h	2.4, 2.4
Clindamycin	75	150-450 mg every 6-8 h	1.5
Doxycycline§	25 (suspension), 25 (syrup)	100 mg every 12 h	1.7, 4.4
Erythromycin	200, 400	250-500 mg every 6 h	3.0, 3.0
Levofloxacin§	125	250-750 mg daily	2.5
Penicillin VK¶	125, 250	250-500 mg every 6-8 h	2.7, 2.7
Analgesics and Anti-inflammatories			
Acetaminophen	160	325-650 mg every 6-8 h	2.5
Acetaminophen with codeine	120-12	325-650 mg every 6-8 h (acetaminophen)	3.0
Codeine	30	15-60 mg every 4 h as needed	4.3
Ibuprofen	100	200-400 mg every 4-6 h	1.6
Miscellaneous			
Diphenhydramine	12.5	25-50 mg every 6-8 h	0.42
Dexamethasone	0.5, 5	4-10 mg every 12 h	1.7, 3.2
Nystatin	500,000 U/5 mL	1-5 mL every 6 h	2.5
Prednisolone	15	Titrated to the individual	1.9
Prednisone	5	Titrated to the individual	0.8

* mg: Milligram.
† mL: Milliliter.
‡ g: Gram.
§ Personal communication from the manufacturer.
¶ Can be brand specific (Stada brand = 2.6 g/5 mL and 2.6 g/5 mL, respectively; Bristol-Myers Squibb brand = 3.5 g/5 mL and 3.5 g/5 mL, respectively).

Encapsulating medicines in solid oral dose forms such as capsules or tablets is an effective method to avoid unpleasant medication tastes, but these formulations can be problematic for patients who have trouble swallowing. Patients with pathologies that are aggravated by medications that irritate the oral mucosa (such as patients undergoing radiotherapy to the oral cavity or chemotherapy), those with feeding tubes in place, or patients who simply cannot swallow tablets or capsules may be better suited for liquid formulations of medications, such as oral solutions or suspensions. These patients pose a significant challenge for oral health care providers (OHCPs), who may prescribe (or who may treat patients who have been prescribed) sugar-containing oral liquid medications.

Here we review the sugar content of oral liquid medications commonly prescribed by OHCPs with consideration to their caries potential. Because the oral cavity is a potential source of sepsis, early and definitive dental intervention, comprehensive oral hygiene measures, and elimination of the cause will reduce the risk for oral and associated systemic complications.[7-10] We focus specifically on some of the most common sugar-containing oral liquid medications patients may be exposed to; we review their oral health implications; and we provide guidance for contemporary dental practice.

DISCUSSION

OHCPs who are prepared with evidence-based information about the formulation of liquid medications can advise their patients regarding optimal medication therapy, potentially helping to ensure healthy outcomes. We based this literature review on searches of the following knowledge-based resources without any restrictions on dates of publication: Medline, PubMed, Embase, and the Cochrane Database of Systematic Reviews. The search terms were "dental care" and "dentistry"; "cariogenicity" and "sugar

ABBREVIATION KEY. **OHCP:** Oral health care provider.

content"; and "patient safety." In addition, we also evaluated journals, Web sites, textbooks, studies, reports, conference proceedings, consensus statements, and abstracts published in English. Multiple pharmaceutical manufacturers were contacted directly with a request to help by providing missing or unpublished data points.

Table 1 lists sugar-containing oral liquid medications commonly prescribed by OHCPs. These medications may be ideal for patients with swallowing difficulties who cannot manage solid oral dosage formulations; however, each medication listed may contain sugar in varying amounts, up to 4 grams per dose (usually 1 teaspoon or 5 milliliters). It should be noted that 1 teaspoon of granulated white sugar equals 4 g of carbohydrates. Because carbohydrates have 4 calories per gram, this equals 16 calories. In a patient who may consume 1,600 calories per day and takes such a medication 4 times a day, then 64 calories per day, or 4% of his or her total daily energy (E) intake, is from the sugar in this medication. A recent meta-analysis suggests that sugar consumption should be limited to < 5% E to minimize the risk of dental caries throughout a patients' life.[15] Patients who are required to take multiple doses per day of these sugar-containing oral liquid medications may be at high risk for drug-induced cariogenicity and associated oral health consequences as a result of the consumption of these medicines and the unknown ingestion of several extra teaspoons of sugar per day.

Table 2 lists sugar-containing oral liquid medications that are not commonly prescribed by OHCPs but that are commonly prescribed by physicians for patients whom OHCPs may be treating for oral health care concerns, such as caries. Given the nature of some diagnoses (for example, patients with head and neck cancers undergoing radiotherapy, organ transplant recipients, patients with human immunodeficiency virus infections, and patients with Sjögren syndrome), oral adverse events such as cariogenicity may be overlooked as drug-associated effects because these patients are typically immunocompromised and the sugar content of many medications is assumed to be negligible compared with the patients' overall dietary intake of sugar. Three minicases are included as examples (Boxes 1-3).

Because the oral cavity can be a source of sepsis, early and definitive dental intervention, comprehensive oral hygiene measures, and elimination of the cause of caries will reduce the risk for oral and associated systemic complications.[7-10] OHCPs may

TABLE 2

Sugar-containing oral liquid medications not commonly prescribed by oral health care providers.[12-15]

MEDICATION	ACTIVE INGREDIENT CONCENTRATION AVAILABLE, mg*/5 mL†	USUAL ADULT DOSE	SUCROSE CONTENT, g‡/5 mL
Alendronate	70	70 mg weekly	None
Amantadine	50	100-400 mg 2 times a day	2.2
Aripiprazole	5	10-30 mg daily	2.0
Bicitra (Sodium Citrate–Citric Acid)	5 milliequivalents/5 mL	10-30 mL 4 times a day	1.15
Carbamazepine	100	100-400 mg 2 to 4 times a day	3.4
Cetirizine	5	5-10 mg daily	2.0
Diazepam	5	Titrated to the individual	1.0
Famotidine	40	20 mg 2 times a day	1.2
Fluconazole	50, 200	200-400 mg daily	2.9, 2.7
Fluoxetine§	20	20-80 mg daily	4.0
Levetiracetam	500	500-1,500 mg 2 times a day	1.0
Loratadine	5	10 mg daily	3.0
Maalox Suspension	500-500	10-20 mL 4 times a day as needed	0.4
Methadone Concentrate	10 mg/mL	Titrated to the individual	0.9
Methadone Sugar-Free Oral Concentrate	10 mg/mL	Titrated to the individual	None
Milk of Magnesia	100	5-15 mL 4 times a day as needed	None
NyQuil	216-10	30 mL every 6 h as needed	3.1
Oxybutynin	5	5 mg 2 to 4 times a day	2.4
Paroxetine	5	20-50 mg daily	2.0
Pseudoephedrine	30	60 mg every 4-6 h as needed	2.2
Ranitidine	75	150 mg 2 times a day	0.5
Risperidone	5	Titrated to the individual	None
Robitussin	100	200-400 mg every 4 h as needed	2.3
Robitussin DM	100-10	10-20 mL every 4 h as needed	2.3
Senna	8.8	15 mg daily	3.8
Valproic Acid¶	250	250 mg 2 to 4 times a day	2.8#

* mg: Milligrams.
† mL: Milliliters.
‡ g: Grams.
§ Can be brand specific (Pharmaceutical Associates brand = 4.0 g/5 mL; Dista brand = 3.0 g/5 mL).
¶ Personal communication from the manufacturer.
# Can be brand specific (Wockhardt brand = 3.0 g/5 mL; Abbott brand = 4.3 g/5 mL).

BOX 1

Minicase 1: oral liquid antibiotics (amoxicillin and cephalexin).

An at-risk patient is scheduled for a dental procedure requiring prophylactic antibiotics per the American Heart Association's current recommendations.[16,17] A one-time dose of amoxicillin is one of the first-line agents. Further consideration is given to more aggressive, ongoing antibiotic therapy in the presence of infection and other comorbidities in this patient, and the typical adult dose of 500 milligrams 3 times a day for 10 days is prescribed.

If the patient has swallowing difficulties, she may be prescribed 500 mg 3 times a day of the amoxicillin 250 mg/5 milliliters oral liquid for 10 days. Each dose contains 3.7 grams of sugar (1.85 g/5 mL × 10 mL). Three doses a day would therefore equate to 11.1 g of sugar—a total of 111 g over the full course of treatment, based on the data in Table 1.

If cephalexin were substituted for amoxicillin in a patient with a potential allergic history to penicillin-type medications, 500 mg 3 times a day of the 250 mg/5 mL oral liquid would result in the ingestion of 12 g of sugar per day, or a total of 120 g over the full course of treatment.

BOX 2

Minicase 2: oral liquid antifungal (nystatin).

A patient presents to the dental office with multiple comorbidities to include poor oral health of several years' neglect. In addition to surgical treatment, oral thrush (candidiasis) is diagnosed, and a prescription for the topical antifungal nystatin is written.

Nystatin oral suspension is indicated for the treatment of candidiasis in the oral cavity. In adults, it is typically administered as a 5-milliliter swish-and-swallow treatment that needs to be taken 4 times a day for up to 10 days.

According to the product label, nystatin contains 50% weight per volume of sucrose, which is the equivalent of 2.5 grams of sugar per each 5-mL dose.[18] In this dental patient with an opportunistic infection of oral thrush, given the high sugar content and mode of delivery, nystatin use creates ideal conditions for causing tooth decay, including extended presence of sugar in the oral environment—in this case, 10 milligrams per day in addition to the patient's regular dietary sugar intake.

BOX 3

Minicase 3: oral liquid analgesics (codeine and methadone).

A patient presents to the dental office for surgical extraction of wisdom teeth. The patient has multiple drug allergies and swallowing difficulties that limit the postoperative analgesic selection to liquid narcotics only. Codeine is a centrally acting narcotic analgesic that is often used to manage moderately severe or severe postoperative dental pain. Codeine sulfate oral solution (30 milligrams/5 milliliters) is available as an orange-flavored, clear, reddish-orange to orange solution, and the usual adult dosage is 15 to 60 mg (2.5 to 10 mL) repeated up to every 4 hours as needed for pain. The maximum recommended 24-hour dose is 360 mg. There are 4.3 grams of sugar in every 5-mL (30-mg) dose, so the patient receives approximately a teaspoon of sugar with every 30-mg dose she receives.

As an alternative to codeine, methadone is also an opioid analgesic indicated for moderate to severe pain.[19] Methadone oral liquid (10 mg/mL) does contain 0.9 g of sugar in each 5 mL of solution; however, it is also available as a sugar-free concentrate (10 mg/mL), which is far less cariogenic.

prescribe antibiotics to patients, or they may be treating patients who are already receiving antibiotics. In patients who have recently received antibiotic therapy and who have developed opportunistic infections such as oral candidiasis, treatment with an antifungal agent may be indicated. In the case of cancer patients with significant pain, opioid and nonopioid-based analgesics are often required for disease management. In each of these examples, sugar-containing oral liquid medications may be prescribed, especially if these patients have swallowing difficulties.

Because of the complexity of some patients' diagnoses (including immunocompromised oncology patients, transplant recipients, and patients with human immunodeficiency virus, Parkinson disease, and Alzheimer disease), the patients may have difficulties practicing effective oral hygiene. These challenges can result in oral adverse events such as cariogenicity being overlooked as drug-associated effects because the sugar content of many medications is assumed to be negligible compared with the patients' overall dietary intake of sugar. There are, however, several medications with a significantly high sugar content that may be associated with negative oral health sequelae, and these should be considered as part of the OHCPs' differential diagnosis of oral pathologies (Tables 1 and 2). If dry mouth is an additional confounder, many of the medications presented here do have xerostomia as an adverse effect, which can further complicate this disease burden.[20]

Some physicians may not be aware that frequently used medications with high sugar content can have a high cariogenic risk. We found over 50 commonly used oral liquid medications to contain varying amounts of sugar, up to 4 g per dose (usually 1 teaspoon or 5 mL). Patients who are required to take multiple doses per day of these sugar-containing oral liquid medications because of swallowing issues may be at the highest risk for drug-induced cariogenicity and associated oral health consequences. Although alternative sweeteners such as sorbitol and xylitol are increasingly common in medicinal preparations in lieu of sucrose,[5] some of these noncariogenic sweeteners, such as saccharin, aspartame, and cyclamate, have a bitter or metallic taste.[6] Regardless, OHCPs may want to consider suggesting sugarless or alternative-sweetener–containing oral liquid preparations if they are available for patients who present with these iatrogenic findings. In lieu of commercially available alternatives, compounding pharmacies are an excellent resource for creating nonsugar-containing oral liquid medications. Patients should also be counseled to rinse their mouths with water or brush their teeth after each dose of these medications to help mitigate cariogenic risk.

CONCLUSIONS

Recognition and avoidance of sugar-containing oral liquid medications can help clinicians optimize patient treatment and decrease drug-induced cariogenicity risk while emphasizing patient safety and improved oral health. Several pharmaceutical manufacturers were

contacted directly for information about the sugar content of their oral liquid formulations during the preparation of this article. Many of the medications listed may have more than one manufacturer, in which case we have reported examples of differences in sugar content, as it may vary according to brand. Some manufacturers refused to provide this information, citing the confidential nature of this proprietary information. Regardless, in reviewing the literature on this subject, we were unable to find a more comprehensive and up-to-date compilation of these data, which may be of high value to practicing OHCPs. ■

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