
Understanding Drug Interactions in Dental Practice

Money Makes the World Go Round, But Drugs Can Make it Spin!

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Our Clinician:



Dr. Mark Donaldson BSP, RPH, PHARMD, FASHP, FACHE received his baccalaureate degree from the University of British Columbia and his Doctorate in Clinical Pharmacy from the University of Washington. He completed a residency at Vancouver General Hospital, and has practiced as a clinical pharmacy specialist, clinical coordinator and director of pharmacy services at many healthcare organizations in both Canada and the United States. He is currently the Associate Vice President of Clinical Pharmacy for Vizient's Advisory Solutions, and lives in Whitefish, Montana.

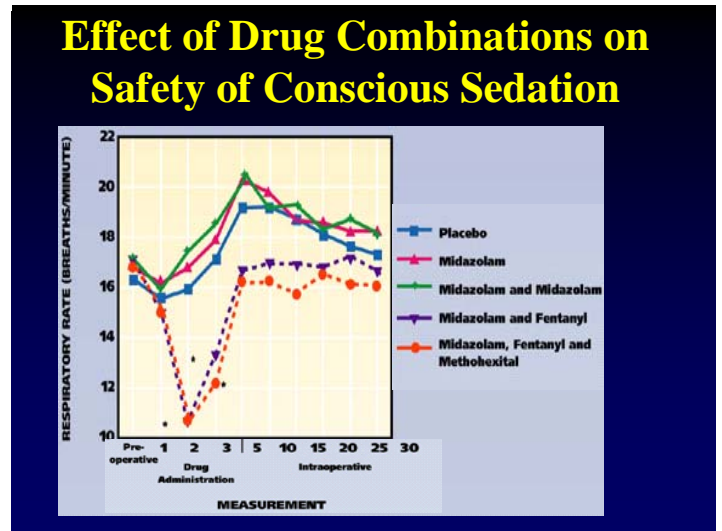
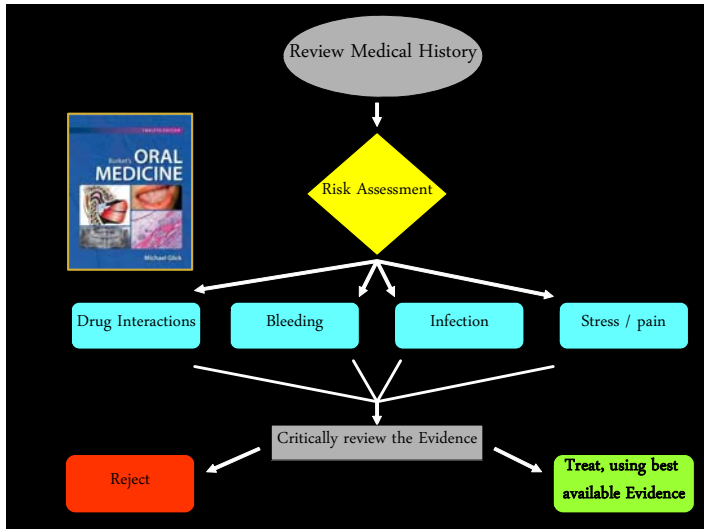
Dr. Donaldson is a Clinical Professor in the Department of Pharmacy at the University of Montana in Missoula, Clinical Associate Professor in the School of Dentistry at the Oregon Health & Sciences University in Portland, Oregon, and affiliate faculty in the School of Dentistry at UBC. He has a special interest in dental pharmacology and has lectured internationally to both dental and medical practitioners. He has spent the last 20 years focusing on dental pharmacology and dental therapeutics, and is a leader in the field.

Dr. Donaldson has published numerous peer-reviewed works and textbook chapters. He currently serves on the Editorial Board for the Journal Healthcare Executive and the Journal of the American Dental Association and is a reviewer for over ten other different journals. He is board certified in healthcare management and is the Past-President and current Regent of the American College of Healthcare Executives' Montana Chapter. Dr. Donaldson was named as the 2014 recipient of the Bowl of Hygeia for the state of Montana and is the 2016 recipient of the Dr. Thaddeus V. Weclaw Award. This award is conferred by the Academy of General Dentistry upon an individual who has made outstanding contributions to the medical, dental and pharmacy literature. Next week, Dr. Donaldson is to be conferred by the Canadian Dental Association (CDA) in Ottawa with the, "Special Friend of Canadian Dentistry Award for 2019." This award is given to an individual outside of the dental profession in appreciation for exemplary support or service to Canadian dentistry and/or to the profession as a whole.

Money Makes the World Go Around, But Drugs Can Make it Spin!

The goal of oral conscious sedation is to create, by pharmacologic or other means, a comfortable environment such that the patient can safely and effectively receive dental care.

There is an inverse relationship between the depth of sedation and the degree of safety associated with it. Clearly, general anesthesia and deep sedation hold the greatest risk of serious morbidity and mortality as well as the highest efficacy. On the other hand, nitrous oxide and oral conscious sedation have the lowest risk and a lower clinical efficacy.



Multiple Agent Protocols

When benzodiazepines are administered alone, only mild changes occur in respiratory rate and oxygen saturation levels. However, adding a barbiturate or a narcotic in a multiple drug regimen with a benzodiazepine creates a statistically significant decrease in both respiratory parameters.

Why should drug interactions concern me? - because polypharmacy is the norm especially in those patients over 65 years old. A Canadian Medical Association policy survey showed that more than 20% of acute care hospital admissions for seniors may result directly from adverse drug reactions. Polypharmacy is used as: complementary therapy; co-morbid conditions and; non-comorbid conditions.

Many of our patients are on multiple drug regimens. **The potential for drug interactions increases dramatically with the number of medications prescribed.**

Chronic illness leads to polypharmacy so that there is a high probability of a drug interaction. But how is this related to dentistry? Almost all of your patients will be on some kind of medication (prescription, OTC, herbals, supplements, recreational). And just because dentists prescribe less than 10% of all available drugs, your patients may be taking others from the 90% you're not familiar with, and not all of your patients will tell you what they are taking. So who is more "at risk" - you or your patient?

"67% of patients do not discuss complementary and alternative medicine (CAM) with their health care providers because the clinicians did not ask."

<http://nccam.nih.gov/news/camstats/2010/introduction.htm>. (Accessed Sept 7, 2015)

Other Notes or Questions to Ask:

Donaldson M and Touger-Decker R. Dietary supplement interactions with medications used commonly in dentistry. J Am Dent Assoc 2013;144(7):787-94.

Donaldson M, Goodchild JH and Zeigler J. Dental considerations for patients taking weight-loss medications. J Am Dent Assoc 2014;145(1):70-4.

Donaldson M, Touger-Decker R. Vitamin and mineral supplements: Friend or foe when combined with medications? J Am Dent Assoc 2014;145(11):1153-8.

Donaldson M. The Spiderman Principle. J Am Dent Assoc 2011;142(11):1-4.

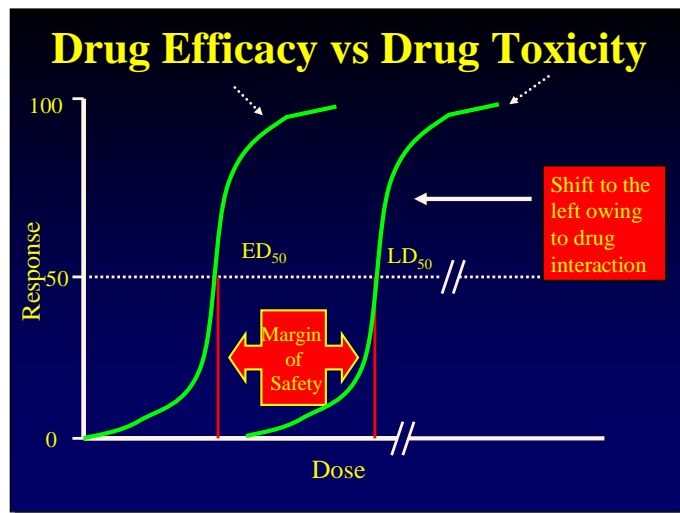
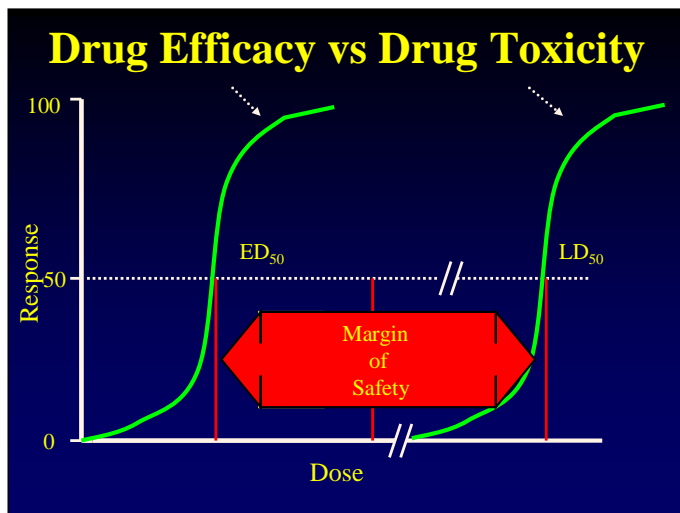
Start with Intrinsically SAFE Drugs (e.g., for sedation)

Most Common	Less Common	Least Common
Nitrous Oxide	Opioids	Barbiturates
Benzodiazepines	Alcohols	Antidepressants
Antihistamines	Phenothiazines	Anticholinergics

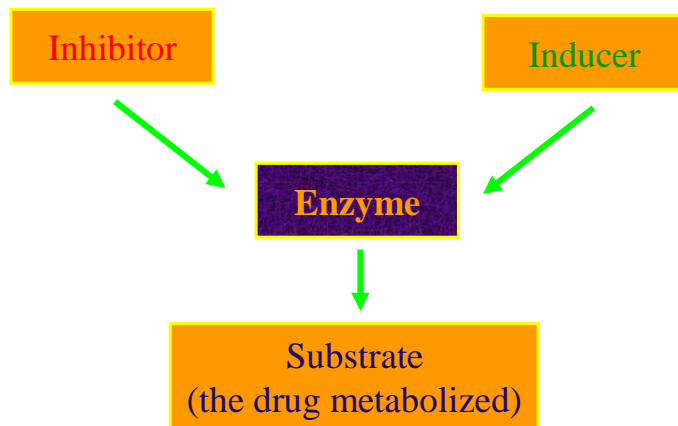
To first understand drug interactions it is important to revisit metabolism. The primary organ of **metabolism** is the liver (although some similar enzymes exist in the cells of the gastrointestinal mucosa). The enzyme complexes in the liver chemically transform the medication molecules into either active or inactive metabolites. These enzymes are known as the **Cytochrome P₄₅₀ (CYP450)** Family of enzymes, and can be further stratified into the individual isoenzymes, which comprise this family. In terms of dental pharmacology, the most prominent isoenzymes to consider are: **CYP3A4, CYP2D6, CYP2C9, CYP1A2 and CYP2C19.**

Metabolism is also known as biotransformation as some drugs are “pro-drugs”. Drug metabolites are usually more polar and less lipid soluble than the parent molecules (this enhances their excretion and distribution half-life). Hepatic oxidation is the major drug metabolizing process. This process, or what the patient does to the drug (pharmacokinetics), and its balance with what the drug does to the body (pharmacodynamics), determines the effectiveness of the medication.

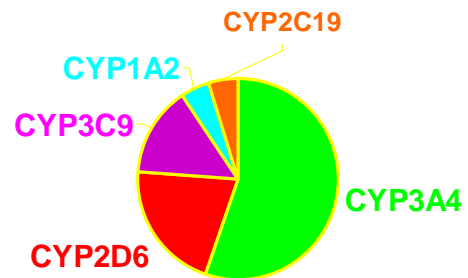
Drug interactions are common causes of treatment failure and adverse reactions. Most drug interactions remain unrecognized because of a wide margin of safety (therapeutic index) compared to inter- and intra-patient variability seen in practice. The effect of inappropriate drug combinations may lead to drug interactions or inaccurate assessment of the clinical effect.



Other Notes or Questions to Ask:



Relative Proportions of Enzymes



It is possible for a drug to be both a substrate and an inhibitor of an enzyme

The therapeutic index of a drug relate its effective dose fifty (ED₅₀) to its lethal dose fifty (LD₅₀) and is a measurement of drug safety. The greater the therapeutic index, the greater the difference between the ED₅₀ and the LD₅₀, the greater the margin of safety. Chloral Hydrate, an alcohol, has a much lower therapeutic index than the benzodiazepine, diazepam. If, however, the two drugs were to be administered together, the LD₅₀ representing the combination would shift significantly to the left, resulting in a much lower degree of safety.

Some points are important to keep in mind:

- ✓ The management of a condition with a drug depends on the predicted effect of that drug
- ✓ The predicted effect depends on the drug being present:
 - in the clinically active dose
 - for the appropriate duration
- ✓ Anything that changes the dose or duration of effect makes drug management unpredictable

Drug interactions give rise to a modified response from the expected or normal response; can cause increased drug levels leading to an enhanced response or increased side effects (clinical relevance depends on the therapeutic indication) or; can cause decreased drug levels leading to sub-clinical or lack of response. Finally, drug interactions can be permanent because of polymorphism (i.e. patient does not have enzyme). **The bottom line is that variability in patient response may be the result of changed metabolism which can be caused by drug interactions.**

Classifying the enzymes responsible for drug metabolism

- Drugs are usually metabolized to inactive metabolites for excretion
- The main route of metabolism for exogenous substances is the liver by the cytochrome P450 mono-oxygenase system
- The P450 system is made up of many enzymes. However, the majority of drug metabolism is by five enzymes: 1A2, 2C9, 2C19, 2D6, and 3A4

There are significant interpatient and inpatient variability with respect to effects of medications and current research indicates that the genetic expression of these liver enzymes may play a prominent role in determining who and why different patients react differently. In the case of isoenzyme CYP2D6, for example, this **genetic polymorphism** in metabolism is common, and can lead to 10 times the difference in drug clearance, leading to either therapeutic failures or increased adverse events and toxicities.

Other Notes or Questions to Ask:

CYP 1A2

Substrate	Inducer	Inhibitor
Caffeine	Carbamazepine	BCPs
Chlordiazepoxide	Clarithromycin	Cimetidine
Diazepam	Cigarette Smoke	Ciprofloxacin
Estrogens	Erythromycin	Fluvoxamine
Haloperidol	Insulin	Isoniazid
Las	Lansoprazole	Ticlopidine
Olanzapine	Omeprazole	
Propranolol	Phenobarbital	
Tamoxifen	Phenytoin	
TCAs	Rifampin	
Theophylline	Ritonavir	

CYP 2C9

Substrate	Inducer	Inhibitor
ASA	Carbamazepine	Amiodarone
Dapsone	Phenobarbital	Azole Antifungals
Diazepam	Phenytoin	Cimetidine (weak)
Dicoumarol	Rifampin	Fluvoxamine
Fluoxetine		Omeprazole
Losartan		Ritonavir
Most NSAIDs		"Statins"
Phenobarbital		Tolbutamide
Phenytoin		
Sulfonamides		
Temazepam		
Tolbutamide		
Zidovudine		

The ultrarapid metabolizer phenotype (where CYP2D6 activity is overactive) leads to a reduced effectiveness of drug at standard doses. The prevalence of this polymorphism among different patient populations is Northern European countries (2%-4%); Mediterranean area (7%-12%); Ethiopians, (29%) and; Saudi Arabian (21%). Conversely, 5%-10% of the Caucasian population have a CYP2D6 deficiency which often leads to an increased potential for drug interactions and side effects due to an accumulation of CYP2D6 metabolized drugs and higher serum drug concentrations, despite administration of "standard doses".

CYP 2C19

Substrate	Inducer	Inhibitor
Barbiturates	Carbamazepine	Azole Antifungals
Diazepam	Norethindrone	Cimetidine (weak)
Lansoprazole	Phenobarbital	Fluoxetine
Omeprazole	Phenytoin	Fluvoxamine
Phenytoin	Prednisone	Lansoprazole
Propranolol	Rifampin	Omeprazole
TCAs		Paroxetine
Temazepam		Ritonavir
Valproic Acid		Ticlopidine
Zidovudine		

CYP 2D6

Substrate	Inducer	Inhibitor
Several β -Blockers	None Known	Amiodarone
Codeine		Cimetidine
Dextromethorphan		Chlorpheniramine
Encainide, Flecainide		Encainide
Haloperidol		Fluoxetine
Halothane		Haloperidol
Hydrocodone		Ketoconazole
MDMA (Ecstasy)		Nefazodone
Omeprazole		Paroxetine
Phenothiazines		Phenothiazines
Propafenone		Quinidine
Selegiline		Ritonavir
SSRIs, TCAs		Sertraline
Venlafaxine		"Statins"
		TCAs
		Venlafaxine

Clinical Relevance of Drug Interactions

- Drug interactions can be caused by enzyme induction, inhibition, or competition
- If an enzyme is induced by a drug, metabolism occurs faster (e.g. Phenobarbital)
- If inhibition occurs the drug is not metabolized as fast (increased blood levels)
 - Two or more drugs (competing for) the same enzyme will lead to variations in blood levels

Other Notes or Questions to Ask:

Case Study #1

A 45 year old woman has been using diazepam intermittently. She has suffered from GERD for 5 years. Her reflux symptoms are controlled by omeprazole but she has recently begun to feel drowsy. She asks if this can be caused by the drugs that she is taking.

Omeprazole is metabolized by CYP 3A4 and by CYP 2C19 and has many interactions with the P450 enzyme system. Omeprazole inhibits the metabolism of drugs (such as diazepam) which are metabolized by CYP 2C19, which can result in increased plasma concentrations.

Not all drugs in the same class are metabolized by the same pathway. Thus when prescribing a second or subsequent drug, potential drug interactions should be considered and drug choice made accordingly. Where a drug interaction occurs, it is often possible to select another drug in the same drug class with a different metabolic pathway. Note that there is also polymorphism with CYP 2C19. 2-6% of Asians do not have the enzyme and are therefore poor metabolizers.

Case Study #2

28 year old female who presents for hygiene, operative, and extraction of her wisdom teeth. Past medical history includes: Depression, Social anxiety disorder and Asthma. She takes Prozac, and albuterol prn. She has NKDA. Surgery went well and she is given codeine syrup postoperatively because, “tablets make me gag.”

That night there is a frantic phone call to the after-hour service from mother, “my daughter is in excruciating pain!” Recommendation given to double codeine dose to 60mg every six hours and if there is still no relief to come back to the office the following day. Patient presents to the office the next morning in tears and obvious pain. No noticeable abscess or swelling . . . What could be going on?? Codeine is a “prodrug” that requires “activation” by the liver. The CYP 2D6 isoenzyme is responsible for converting codeine to its active form, morphine (*Br J Anaesth 2002; 89: 839–45*).

Up to 10% of the Caucasian population have a deficiency in this isoenzymes so they cannot activate codeine. Since pain of dental origin is primarily related to inflammation and narcotics like codeine are not antiinflammatory agents, ibuprofen and acetaminophen should be the combination of choice (helps avoid “codeine failures” also).

Donaldson M and Goodchild JH. Appropriate analgesic prescribing for the general dentist. Gen Dent 2010; 58(4):291-7.

Case Study #3

A 73-year old man who has been on lovastatin (Mevacor®) 20mg daily for the past seven years is given six courses of erythromycin (9 grams over 2 weeks) for subacute bacterial endocarditis (SBE) prophylaxis. Most of the procedures involved simple crowns and fillings. Doses were all appropriate as per the old American Heart Association guidelines (*J Am Dent Assoc. 1997 Aug;128(8):1142-51*).

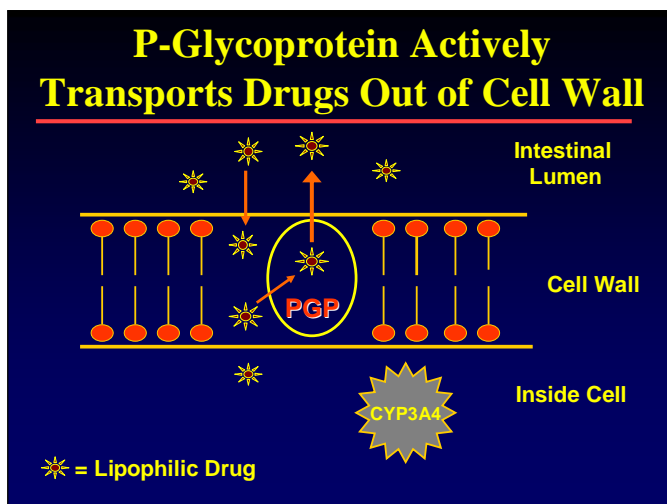
One day after his last erythromycin dose he experiences generalized muscular weakness, anorexia, nausea and vomiting. Four days after his last erythromycin dose he presents to the Emergency Room at his local hospital complaining of muscle weakness with noticeable abdominal distension. He was admitted to hospital and rapidly deteriorated, developing rhabdomyolysis, acute renal failure, pancreatitis, ileus, and elevated liver function tests.

CYP 3A4		
Substrate	Inducer	Inhibitor
Alprazolam	Barbiturates	CCBs (esp. Diltiazem)
Astemizole	Cyclophosphamide	Clarithromycin
Atorvastatin	Dexamethasone	Corticosteroids
Barbiturates	Lansoprazole	Cyclosporine
CCBs (not diltiazem)	Omeprazole	Erythromycin
Cisapride	Phenytoin	Fluconazole
Clarithromycin	Rifampin	Fluoxetine
Cyclosporine	Sex Steroids	Fluvoxamine
Erythromycin		Grapefruit Juice
Fentanyl, Halothane		Itraconazole
HIV Protease Inhibitors		Ketoconazole
Loratidine, Lovastatin		Lansoprazole
Midazolam, SSRIs		Midazolam
Simvastatin, TCAs		Nefazodone
Terfenadine, Triazolam		Omeprazole
		Tamoxifen
		TCAs

Other Notes or Questions to Ask:

He spent the next ten days in the intensive care unit, where his condition ultimately stabilized and the severity of his condition was down-graded as slow improvements were noted. It took a further seven days as hospital inpatient before he had recovered enough to be appropriately discharged. Happily he survived the ordeal.

Oral Erythromycin and the Risk of Sudden Cardiac Death (*NEJM 2004;351:1089-96*): “The adjusted rate of sudden death from cardiac causes was twice as high as placebo and amoxicillin . . . The adjusted rate of sudden death from cardiac causes was 5 times as high among those who concurrently used CYP3A4 inhibitors.” “During 5 days of azithromycin therapy, there was a small absolute increase in cardiovascular deaths, which was most pronounced among patients with a high baseline risk of cardiovascular disease (*NEJM 2012; 366:1881-1890*).



P-glycoprotein (P-gp)

- ✓ Efflux pump: ↓ exposure to xenobiotics
- ✓ Found in numerous tissues:
 - Intestinal epithelium
 - Biliary canaliculi
 - Renal proximal tubules
 - Blood-brain barrier
 - Tumor Cells
- ✓ Promiscuous: interacts with wide variety of chemical structures

Kovarik JM et al. Clin Pharmacol Ther 1999;66:391-400

Grapefruit Juice is considered a **Suicide Inhibitor** because it completely destroys some of the CYP3A4 in the small intestine. Normal enzyme levels of this isoenzyme are reestablished after body makes more, usually in 2 to 3 days after the juice leaves body. Juice from the frozen concentrate is a more potent inhibitor than fresh juice or 1/2 grapefruit.

Besides the liver, metabolism also occurs in other parts of the body such as: the intestinal epithelium, biliary canaliculi, renal proximal tubules, blood-brain barrier, and some tumor cells. The mechanism responsible for this is the **P-Glycoprotein** efflux pump, which has gained particular notoriety in explaining the interaction between grapefruit juice and some medications.

There are, of course, risk factors for drug interactions. The high risk situations are: administration to the very young and elderly; administration to medically compromised patients; the use of chronic drug therapies involving drugs that are excreted slowly and; the use of drugs with small margins of safety:

digoxin, warfarin, opioids, lithium, theophylline, thyroid medications

Other points to note: The majority of drug interactions occur with chronic therapy (antibiotics are the exception) and; most drug interactions occur with cardiovascular, NSAIDs and CNS drugs.

Summary

- Be careful: titrate to minimize the possibility of severe reaction occurring (go low, go slow)
- Be aware: If patients come back and say, “I don’t feel well on this medication”, drug interactions should be one of your considerations
- The less that a drug is metabolized, the lower the chance of a drug interaction
- If the drug is not producing the anticipated results, altered metabolism is a possibility (whether inhibition, or induction of the substrate or absence of the enzyme)

Other Notes or Questions to Ask:

- In polypharmacology, drugs with fewer potential drug interactions should always be considered (e.g., Escitalopram, pantoprazole, other...)

Unique Characteristics of Dental Therapeutics

- Usually single dose or short-term therapy (5-10 days)
- Most dental drugs have large margin of safety
- Use of IV drugs is limited
- Procedures are usually elective
- Drug armamentarium is limited

There are numerous potentially dangerous medication interactions and clinically significant factors to consider:

- Metronidazole and Alcohol
- Watch for duplications
- Tetracycline and certain cations
- Ask about ALL the drugs your patient takes
- Antibiotics and Birth Control Pills
- Consider theoretical vs. clinical significance
- NSAIDS & ASA and Warfarin
- Consider age, weight, renal and liver function
- Always consider a drug's therapeutic index

Lexi-Comp's Drug Information Handbook for Dentistry: Oral Medicine for Medically-Compromised Patients and Specific Oral Conditions is one of the most compact text references available. This resource contains abbreviated monographs on prescription medications and is well known for its useful charts and comparison tables. It is easy to use and is organized in alphabetical order according to a drug's generic name. The handbook provides useful information when looking for a quick response to a simple drug information request, such as indications, dosages, general adverse effects, and drug interactions. The *Drug Information Handbook* provides an updated edition annually to include new drugs and updates to current medications.

Physicians' Desk Reference (PDR): The *PDR* is a compilation of drug package inserts. It does not include all prescription medications because of space limitations. A new *PDR* is published every year; however, it is important to note that the information may not be updated with each annual publication. It is also important to note that only FDA-approved indications and dosages can be found within the *PDR*.

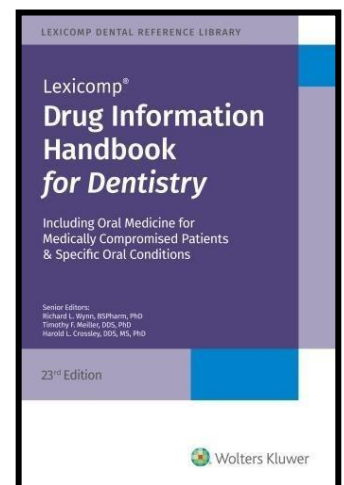
Lexi-Comp Online: In addition to the compact handbook, Lexi-Comp also provides Web-based and PDA resources with annual subscriptions. Lexi-Comp Online offers a convenient way to search medications quickly and easily. Once a medication is searched, the user can scroll through various parts of the drug monograph using the simple drop-down menu. This allows the user to move from section to section with ease and speed. Other features included are a drug-interaction reviewing tool, patient education leaflets, a drug-identification database, lists of drug recalls and shortages, and recent drug news.

Micromedex: Micromedex is a popular Web-based resource. Using one search box, a clinician is able to search many different databases that include detailed and summarized drug information, toxicology, alternative medicine, and reproductive risk evaluation. Micromedex's detailed information highlights Drugdex, *PDR*, and

Other Notes or Questions to Ask:

Consider Your Resources

- Texts ([Lexicomp's Drug Information Handbook for Dentists](#))
- [Lexicomp Dental Drug Database](#)
- [Web-based Services \(Drug Reax by Micromedex\)](#)
- www.naturaldatabase.com
- [Clinical Pharmacology by Gold Standard Multimedia](#)
- order1@adecllc.info by Dr. Michael Glick
- PDAs (Epocrates, Tarascon and others)



Martindale's (for use in searching foreign medications). The toxicology information that is included with these resources is trademarked as *Poisindex* and *Identidex*. Poisindex identifies ingredients for commercial, biological, and pharmaceutical products and delivers summarized toxicology data. Identidex allows the clinician to identify a medication using its embossed lettering or numbering and other descriptive characteristics, such as color and shape. Other useful tools in this resource include a drug interaction reviewing tool, patient education leaflets for both prescription drugs and dietary supplements, and clinical calculators to help determine body mass index, ideal body weight, metric conversions, and others.

Clinical Pharmacology: Clinical Pharmacology is a Web-based application providing a vast array of information that is both thorough and practical. It has multiple functions, allowing users to obtain product information, view monographs, identify medications, and print patient education materials. The site also contains drug class overviews, various interactions (including drug–drug, drug–herbal, drug–nutritional, and drug–food interactions), and full-color product images.

ICE's Medical Support System, a website providing resources on medical conditions as they relate to oral health care. "This unique software will enhance oral health care professionals' ability to help a patient population that presents with medical conditions that impact the provision of dental care," said Dr. Michael Glick, author of the content on the site. Dr. Glick is professor of oral medicine and dean, School of Dental Medicine, University at Buffalo, N.Y., and editor of The Journal of the American Dental Association. The site is located at "www.icemedicalsupport.com".

The Medical Support System provides up-to-date, point-of-care oral care information that is continually updated in more than 50 languages. Using the information available on the site, dentists and other dental team members can assess a patient's potential for medical complications and the need for dental modifications. Additionally, subscribers can amass up to three hours of continuing education credits through use of the site. A demo of the site is available at www.icemedicalsupport.com/demo. For more information about the Medical Support System, visit <http://icemedicalsupport.com/ada> or you can call 1-866-292-9725 or email info@icehealthsystems.com.

Other Notes or Questions to Ask:

Herbal Interactions


All cultures on all continents have herbal healing traditions. Until the 20th century, most people everywhere had close contact with foods and herbs where they were grown. Through the 1930s, MDs in US studied and relied on plant drugs as primary medicines. Medical schools taught plant taxonomy and medicinal plant therapeutics (pharmacognosy). In 1870, the US Pharmacopeia listed 636 herbal entries. The 1990 edition listed 58. Some were found unsafe, most were replaced by pharmaceuticals.

Dietary Supplement Health and Education Act of 1994 (DSHEA) allows 4 types of statements:

1. Role of nutrient in affecting “structure and function” in humans.
2. Documented mechanism that supplement acts on to affect “structure and function”.
3. Benefits due to dietary deficiency-must report the prevalence of disease in USA.
4. Statements of general well-being from consumption of the supplement.

Depression Example:	Treat depression	No
	Elevate mood	Yes
Vitamin A is essential to proper eye function		Yes
Calcium is essential for bone health		Yes
Saw palmetto promotes prostate health		Yes

Herbal Practitioners Today

- In US today, herbal practice can include:
 - Herbalists in family or cultural traditions
 - Native American medicine men and women
 - Latino Curanderos
 - American Herbalist Guild members
 - Self-taught lay herbalists
 - Naturopathic physicians
 - L.Acs with training in Chinese herbs
 - Licensed Acupuncturists
 - MDs, DOs, DCs with specific interest in herbs
 - Ayurvedic doctors
 - The God of Ayurveda Dhanvantari → 
 - Self-prescribers

But “disease” claims not permitted:

Saw palmetto cures or relieves BPH: Not OK
 CardioHealth: OK, Hepaticure: Not OK
 “Reduces the stiffness of arthritis” not permitted
 “Promotes joint health” is permitted

Depending on state law, these kinds of distinctions may also apply to health care practitioners such as chiropractors. Any structure/function claims must also include:

“This statement has not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease”

Under the US Dietary Supplement Health and Education Act of 1994, the FDA can:

- Promulgate good manufacturing practices.
- Refer for criminal action the sale of toxic products.
- Obtain injunction against false claims.
- Seize products that pose unreasonable risk
- Sue company making claims of cure or treating disease.

The FDA cannot regulate supplements as drugs, requiring the same level of proof of efficacy in order for the supplements to be marketed (this applies to vitamins, minerals, herbs, nutraceuticals etc.). The FDA is therefore developing the National Center for Complementary and Alternative Medicine (NCCAM) which can deal with issues of safety, labeling, enforcement, science based research so that some self-regulation/standards exist.



Other Notes or Questions to Ask:

Up to 42% of Americans are using some sort of dietary supplement for both prevention and therapeutic purposes, 26.8 billion dollar industry in 2018.

1. General Health
2. Colds
3. Arthritis
4. Energy Enhancement
5. Cholesterol Lowering
6. Cancer Prevention
7. Allergies
8. Weight Management


Many conventional medications are derived from herbs:

- 35% prescription drugs
- 60% OTC drugs

Over 50 population: average of 7 or more supplements. Someone turns 50 every 10 seconds in the US.

Differences Between Herbs and Drugs

<u>Drug</u>	<u>Herbals</u>
Dose established	Usually some guidelines
Efficacy proof	Proof of efficacy not required
Monosubstance	Complex compound
FDA-approval before marketing	No FDA pre-approval post-marketing Notification for structure-function claims
Patentable	Not patentable
Potency standardized	Potency varies



Top 20 Selling Herbs (Mass Market HerbalGram)

Common Name	Latin Name
1. Garlic	1. Allium sativum
2. Echinacea	2. Echinacea spp.
3. Saw palmetto	3. Serenoa repens
4. Ginkgo	4. Ginkgo biloba
5. Cranberry	5. Vaccinium macrocarpon
6. Soy	6. Glycine max
7. Ginseng	7. Panax ginseng
8. Black cohosh	8. Actaea racemosa
9. St. John's wort	9. Hypericum perforatum
10. Milk thistle	10. Silybum marianum
11. Green tea	11. Camellia sinensis
12. Evening primrose	12. Oenothera biennis
13. Valerian	13. Valeriana officinalis
14. Horny goat weed	14. Epimedium spp.
15. Grape seed extract	15. Vitis vinifera
16. Bilberry	16. Vaccinium myrtillus
17. Red clover	17. Trifolium pratense
18. Yohimbine	18. Pausynstalia johimbe
19. Horse chestnut seed extract	19. Aesculus hippocastanum
20. Ginger	20. Zingiber officinalis

Top 20 Selling Herbs (Mass Market HerbalGram)

1. Garlic	11. Green tea
2. Echinacea	12. Evening primrose
3. Saw palmetto	13. Valerian
4. Ginkgo	14. Horny goat weed
5. Cranberry	15. Grape seed extract
6. Soy	16. Bilberry
7. Ginseng	17. Red clover
8. Black cohosh	18. Yohimbine
9. St. John's wort	19. Horse chestnut seed ext.
10. Milk thistle	20. Ginger

Herbals and Dentistry: What are we really worried about?

1. Bleeding / Hemostasis (Patients on Anticoagulants)
2. Thromboembolism (Patients on Blood Thinners)
3. CNS Interactions (Patients who may receive Sedatives)
4. Blood Pressure Issues (Patients who may be receiving Antihypertensives)

Other Notes or Questions to Ask:

Top 20 Selling Herbs that may affect Bleeding / Hemostasis (Patients on Anticoagulants)

- | | |
|--------------------|------------------------------|
| 1. Garlic | 11. Green tea |
| 2. Echinacea | 12. Evening primrose |
| 3. Saw palmetto | 13. Valerian |
| 4. Ginkgo | 14. Horny goat weed |
| 5. Cranberry | 15. Grape seed extract |
| 6. Soy | 16. Bilberry |
| 7. Ginseng | 17. Red clover |
| 8. Black cohosh | 18. Yohimbine |
| 9. St. John's wort | 19. Horse chestnut seed ext. |
| 10. Milk thistle | 20. Ginger |

Honorable mentions: Alfalfa, Beer, Danshen, Dong Quai, EDTA, Glucosamine, Licorice, Policansol, Vitamin K, Willow Bark, Wintergreen.

Top 20 Selling Herbs that may affect Thromboembolism (Patients on Blood Thinners)

- | | |
|--------------------|------------------------------|
| 1. Garlic | 11. Green tea |
| 2. Echinacea | 12. Evening primrose |
| 3. Saw palmetto | 13. Valerian |
| 4. Ginkgo | 14. Horny goat weed |
| 5. Cranberry | 15. Grape seed extract |
| 6. Soy | 16. Bilberry |
| 7. Ginseng | 17. Red clover |
| 8. Black cohosh | 18. Yohimbine |
| 9. St. John's wort | 19. Horse chestnut seed ext. |
| 10. Milk thistle | 20. Ginger |

Honorable mentions: Danshen, Dong Quai, Policansol, Willow Bark

Top 20 Selling Herbs that may affect Blood Pressure (Patients on Antihypertensives)

- | | |
|--------------------|------------------------------|
| 1. Garlic | 11. Green tea |
| 2. Echinacea | 12. Evening primrose |
| 3. Saw palmetto | 13. Valerian |
| 4. Ginkgo | 14. Horny goat weed |
| 5. Cranberry | 15. Grape seed extract |
| 6. Soy | 16. Bilberry |
| 7. Ginseng | 17. Red clover |
| 8. Black cohosh | 18. Yohimbine |
| 9. St. John's wort | 19. Horse chestnut seed ext. |
| 10. Milk thistle | 20. Ginger |

Honorable mentions: Dolomite, Hawthorn, Indian Snakeroot, Oleander, Thuja, Yellow Dock

Top 20 Selling Herbs that may affect Cognition (Patients on Sedatives)

- | | |
|--------------------|------------------------------|
| 1. Garlic | 11. Green tea |
| 2. Echinacea | 12. Evening primrose |
| 3. Saw palmetto | 13. Valerian |
| 4. Ginkgo | 14. Horny goat weed |
| 5. Cranberry | 15. Grape seed extract |
| 6. Soy | 16. Bilberry |
| 7. Ginseng | 17. Red clover |
| 8. Black cohosh | 18. Yohimbine |
| 9. St. John's wort | 19. Horse chestnut seed ext. |
| 10. Milk thistle | 20. Ginger |

Honorable mentions: 5-HTP, Ergot, Hawaiian baby woodrose, Kava Kava, L-tryptophan, Lithium, SAME, Thuja

Top Selling Herbs that are Most Prone to Drug Interactions - Indications

- Garlic – Atherosclerosis; Colorectal & Gastric Cancer; HT
- Echinacea – Common Cold; Vaginal Candidiasis
- Ginkgo – Memory; Dementia; Retinopathy; Glaucoma; PMS
- Soy – Breast CA; Diabetes; Hyperlipidemia; Menopausal symptoms; Osteoporosis
- Ginseng – Diabetes; Respiratory tract infections
- St. John's wort - Depression
- Evening primrose – Mastalgia; Osteoporosis
- Horny goat weed - Osteoporosis
- Yohimbine – Erectile Dysfunction (ED); sexual dysfunction

Other Notes or Questions to Ask:

Top Selling Herbals that are Most Prone to Drug Interactions - EBM

Garlic – Atherosclerosis; HT
Echinacea – No Evidence
Ginkgo – No Evidence
Soy – Possibly Effective
Ginseng – No Evidence
St. John's wort - Depression
Evening primrose – Possible Effective
Horny goat weed – No Evidence
Yohimbine – Possibly Effective

The H.E.R.B.A.L. Mnemonic

- H ear the Patient out with respect
- E ducate the patient
- R ecord and document
- B eware
- A gree to discuss
- L earn about new & popular supplements

Web Resources on Herbs

- American Herbalists Guild:
www.americanherbalistsguild.com
- Herb Research Foundation
www.herbs.org
- Natural Medicines Comprehensive Database
www.naturaldatabase.com
- National Center for Complementary and Alternative Medicine
www.nccam.nih.gov
- Office of Dietary Supplements
www.ods.od.nih.gov

Which Drugs Do You REALLY Have to Worry About?

Warfarin, Cyclosporine, Digoxin, HIV protease inhibitors, Theophylline, Carbamazepine, Lithium, Thyroid medications, Opioids

Steps for Detecting and Advising on Herbal/Drug Interactions

- Is the patient taking any herbal supplements?
- Does the herbal have efficacy for the intended use?
- Is the product reliable? (i.e., what are they REALLY taking?)
- Is the Rx drug one with a narrow therapeutic margin (warfarin, cyclosporine, digoxin, HIV protease inhibitors, theophylline, carbamazepine, lithium, thyroid medications, opioids)?

General Guidelines on Use of Herbal Medicines

- Take a good history of patient use of herbs and supplements.
- Diagnosis needed before using herbs for symptomatic treatment.
- Natural does not equal safe.
- Generally avoid herbs during pregnancy and lactation.
- In children, pay close attention to dosage according to weight.

Other Notes or Questions to Ask:
