

Medications inducing dry mouth and sialorrhea:

A guide released by the World Workshop on Oral Medicine VI

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About 50% of the population is treated with at least one medication and 30% of them develop salivary side-effects. Dry mouth, either subjective (named xerostomia) or objective (salivary gland hypofunction), and sialorrhea (subjective or objective) cause significant morbidity and impair quality of life. The World Workshop on Oral Medicine VI has recently reviewed this subject^{1,2,3,4}, and a list of medications inducing dry mouth and sialorrhea has been compiled and published⁵.

After searching databases for papers with an acceptable degree of relevance, quality of methodology and strength of evidence, we found 106 chemical substances with moderate to high level of evidence of causing dry mouth or sialorrhea. Most drugs are used to treat conditions of the alimentary, cardiovascular, genitourinary, musculoskeletal, nervous and respiratory systems.

While xerostomia was a commonly reported outcome, salivary gland hypofunction and sialorrhea were rarely assessed. The severity of these side-effects is usually dose-dependent and associated with the number of

¹ Dawes C, Pedersen AM, Villa A, Ekström J, Proctor GB, Vissink A, Aframian D, McGowan R, Aliko A, Narayana N, Sia YW, Joshi RK, Beier Jensen S, Kerr AR, Wolff A. The functions of human saliva: A review sponsored by the World Workshop on Oral Medicine VI. *Arch Oral Biol.* 2015;60:863-74.

² Aliko A, Wolff A, Dawes C, Aframian D, Proctor G, Ekström J, Narayana N, Villa A, Sia YW, Joshi RK, McGowan R, Beier Jensen S, Kerr AR, Lynge Pedersen AM, Vissink A. World Workshop on Oral Medicine VI: clinical implications of medication-induced salivary gland dysfunction. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2015;120:185-206

³ Villa A, Wolff A, Aframian D, Vissink A, Ekström J, Proctor G, McGowan R, Narayana N, Aliko A, Sia YW, Joshi RK, Beier Jensen S, Kerr AR, Dawes C, Lynge Pedersen AM. World Workshop on Oral Medicine VI: a systematic review of medication-induced salivary gland dysfunction: prevalence, diagnosis, and treatment. *Clin Oral Investig.* 2015;19:1563-80

⁴ Villa A, Wolff A, Narayana N, Dawes C, Aframian DJ, Lynge Pedersen AM, Vissink A, Aliko A, Sia YW, Joshi RK, McGowan R, Beier Jensen S, Kerr AR, Ekström J, Proctor G. World Workshop on Oral Medicine VI: A systematic review of medication-induced salivary gland dysfunction. *Oral Dis.* 2016; 22:365-382

⁵ Wolff A, Joshi RK, Ekström J, Aframian D, Lynge Pedersen AM, Proctor G, Narayana N, Villa A, Sia YW, Aliko A, McGowan R, Kerr AR, Beier Jensen S, Vissink A, Dawes C. A guide to medications inducing salivary gland dysfunction, xerostomia, and subjective sialorrhea: A systematic review sponsored by the World Workshop on Oral Medicine VI. *Drugs R D.* 2017;17(1):1-28

medications that are consumed. Management strategies include substitution or discontinuation of medications whenever possible, oral or systemic therapy with sialogogues, administration of saliva substitutes, and use of electro-stimulating devices.

It should be noted that this list (1) includes only medications based on one single active ingredient; (2) may exclude some medications that could cause dry mouth or sialorrhea only when given in conjunction with others; (3) may exclude medications that induce dry mouth or sialorrhea but were not detected in our search.

This list may assist practitioners in assessing patients who complain of dry mouth while taking medications. The list may also prove useful for anticipating adverse effects and help practitioners to consider alternative medications. For clinical implementation, it is recommended to use the complete paper, which can be accessed by searching for <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5318321/> and the Anatomical Therapeutic Chemical Classification System of medications (http://www.whocc.no/atc_ddd_index/).

Medications reported to induce xerostomia, salivary gland hypofunction (SGH) or sialorrhea

Drug name	Function	Dry mouth	Sialorrhea
Alendronate	Anti-bone-resorption	x	
Amisulpride	Anti-psychotic	x	
Amitriptyline	Anti-depressant	x	
Aripiprazole	Anti-psychotic	x	
Asenapine	Anti-psychotic	x	
Atenolol	Anti-hypertensive/ Anti- arrhythmic	x	
Atropine	Anti-peristaltic/ Spasmolytic / Mydriatic	x	
Azelastine	Anti-allergic	x	
Baclofen	Skeletal muscle relaxant	x	
Bendroflumethiazide	Diuretic	x	
Bevacizumab	Anti-neoplastic	x	
Brimonidine	Anti-glaucoma	x	
Buprenorphine	Opioid-analgesic	x	
Bupropion	Anti-depressant	x	
Butorphanol	Opioid-analgesic	x	
Cetirizine	Anti-allergic	x	
Clobazam	Anxiolytic/Anti-convulsant		X
Chlorpromazine	Anti-psychotic	x	
Citalopram	Anti-depressant	x	
Clonidine	Anti-hypertensive/ Anti-migraine	x	
Clozapine	Anti-psychotic	x	X
Cyclobenzaprine	Skeletal muscle relaxant	x	
Darifenacin	Urological - reduces bladder activity	x	
Desipramine	Anti-depressant	x	
Desloratadine	Anti-allergic/ Anti-pruritic	x	
Desvenlafaxine	Anti-depressant	x	
Dexfenfluramine	Appetite suppressant	x	
Dexmedetomidine	Hypnotic-sedative	x	
Dexmethyl-phenidate	Psychostimulant (ADHD)	x	
Didanosine	Anti-viral (HIV-1 therapy)	x	
Dihydrocodeine	Opioid-analgesic	x	

Dimebon	Anti-dementia	x	
Dosulepin	Anti-depressant	x	
Doxepin	Anti-depressant	x	
Doxylamine	Hypnotic	x	
Duloxetine	Anti-depressant	x	
Ebastine	Anti-allergic/ Anti-pruritic	x	
Enalapril	Anti-hypertensive	x	X
Escitalopram	Anti-depressant	x	
Eszopiclone	Hypnotic-sedative	x	
Etravirine	Anti-viral (HIV-1 therapy)	x	
Fentanyl	Opioid-analgesic	x	
Fesoterodine	Urological - reduces bladder activity	x	
Fluoxetine	Anti-depressant	x	
Furosemide	Diuretic	x	
Gabapentin	Anti-convulsant	x	
Haloperidol	Anti-psychotic	x	X
Hyoscyamine	Anti-peristaltic/ Spasmolytic	x	
Imidafenacin	Urological - reduces bladder activity	x	
Imipramine	Anti-depressant	x	
Isradipine	Anti-hypertensive	x	
Lamivudine	Anti-viral (HIV-1, hepatitis B therapy)	x	
Levocetirizine	Anti-allergic	x	
Lisdexamfetamine	Psychostimulant (ADHD)	x	
Lisinopril	Anti-hypertensive	x	
Lithium	Anti-psychotic	x	
Loxapine	Anti-psychotic	x	
Lurasidone	Anti-psychotic	x	
Maraviroc	Anti-viral	x	
Methyldopa	Anti-hypertensive	x	X
Methylphenidate	Psychostimulant (ADHD)	x	
Metoprolol	Anti-hypertensive/ Anti- arrhythmic	x	
Mexiletine	Anti-arrhythmic	x	
Morphine	Opioid-analgesic	x	
Naltrexone	Treatment of alcoholism	x	
Nevirapine	Anti-viral (HIV-1 therapy)	x	
Nicotine	Smoking cessation	x	
Nortriptyline	Anti-depressant	x	
Olanzapine	Anti-psychotic	x	X
Orlistat	Anti-obesity	x	
Oxybutynin	Urological - reduces bladder activity	x	
Paliperidone	Anti-psychotic	x	
Paroxetine	Anti-depressant	x	
Perphenazine	Anti-psychotic	x	
Phentermine	Appetite suppressant	x	
Pregabalin	Anti-convulsant	x	
Propantheline	Anti-peristaltic/ Spasmolytic	x	
Propiverine	Urological - reduces bladder activity	x	
Quetiapine	Anti-psychotic	x	X
Raltegravir	Anti-viral (HIV-1 therapy)	x	
Reboxetine	Anti-depressant	x	

Risperidone	Anti-psychotic	x	X
Rotigotine	Anti-Parkinson	x	
Saquinavir	Anti-viral	x	
Sertindole	Anti-psychotic	x	
Scopolamine	Anti-peristaltic/ Spasmolytic / Anti-nauseant/ Sedative	x	
Sertraline	Anti-depressant	x	
Sibutramine	Anti-depressant	x	
Sodium valproate	Anxiolytic/Anti-convulsant	x	
Solifenacin	Urological - reduces bladder activity	x	
Tapentadol	Opioid-analgesic	x	
Terazosin	Urological - decreases urinary flow obstruction / Anti-hypertensive	x	
Tesofensine	Appetite suppressant	x	
Timolol	Anti-glaucoma	x	
Tiotropium	Anti-asthmatic	x	
Tizanidine	Skeletal muscle relaxant	x	
Tolterodine	Urological - reduces bladder activity	x	
Tolvaptan	Diuretic	x	
Tramadol	Opioid-analgesic	x	
Trospium	Urological - reduces bladder activity	x	
Venlafaxine	Anti-depressant	x	
Verapamil	Anti-hypertensive/ Anti-angina	x	
Vortioxetine	Anti-depressant	x	
Ziprasidone	Anti-psychotic	x	
Zolpidem	Hypnotic-sedative	x	
Zopiclone	Hypnotic	x	