Alcohol

(Booze, ethyl or ethanol, adult beverage, brew, brewhski, liquor, drink, shot, sauce, rot gut, hooch, giggle juice, moonshine, jello shots, wobbly pop)

Interaction

a) A case-control study found that NSAID use by individuals who regularly consume more than 5 drinks at a time increased their risk of gastrointestinal complications (e.g., stomach bleeds, ulceration) from 2.8 to 6-fold (odds ratio of GI complications of NSAID alone was 3.8 compared to NSAID non-users).

b) Another case-control study examined the effects associated with the use of prescription NSAIDs or non-prescription naproxen or ibuprofen in individuals with a history of alcohol abuse. Investigators found that the risk ratio of gastrointestinal-associated adverse effects was greater than was predicted by additive risk.

c) A case report describes an alcohol dependent patient who developed methemoglobinemia after taking naproxen sodium for the common cold.

Mechanism

a,b) The mechanism of the increased risk of GI bleed is not well understood but it appears that it is due to the fact NSAIDs and alcohol affect platelet function and bleeding risk.

b) The mechanism is not well understood, nor could the methemoglobinemia be definitively linked to naproxen use, as the patient took other medications as well. It is hypothesized that the methemoglobinemia occurred because alcohol reduces glucose-6-phosphate-dehydrogenase activity, and naproxen causes oxidative stress.

Significance

a,b) Patients should be counselled to avoid binge drinking while taking naproxen.

As both excessive alcohol use and NSAID use are associated with risks for gastrointestinal adverse effects, use of NSAIDs in heavy drinkers is cautioned.

c) The significance of this single case report is unknown. Naproxen should be used cautiously in patients with frequent or heavy alcohol intake.

Think First

Mixing naproxen with alcohol doesn’t change the risk of drinking alcohol. This means, your usual dose of naproxen and 1 or 2 drinks.

remember, 1 drink = 1 beer, 1 glass of wine or 1 shot of liquor.

Serious Risk for Harm

Alcohol can irritate the stomach lining. So can naproxen. Together, they may increase the risk of nausea, stomach pain, or stomach bleeding.

Rarely, binge drinking of alcohol in patients taking medications similar to naproxen has led to severe kidney damage.

Think First

There was a medical case report of a person who frequently drank large amounts of alcohol developed a condition called methemoglobinemia after taking naproxen. This is when your red blood cells are not able to carry enough oxygen, and can cause you to have a headache, be dizzy, have shortness of breath and your skin to have a bluish color temporarily.

Tobacco

(smokes, butts, cigs, cigars, darts, stogies, cancer sticks, chew, dip)

Interaction

According to the product monograph, smokers may be at an increased risk of GI complications of NSAIDs such as ulceration and bleeding.

Significance

NSAIDs should be used with caution in patients who have risk factors for GI complications, such as smoking. If they are used regularly, patients should be monitored for abdominal pain, blood in the stool or vomit, and other signs of GI ulceration or bleeding.

Serious Risk for Harm

People who smoke tobacco are more likely to experience stomach or intestinal problems (like an ulcer or bleeding) when taking naproxen.
Caffeine
(coffee, java, joe, soda, pop, tea, energy drinks (Red Bull®, Monster®, Rock Star®, Amp®, NOS®, Full Throttle®, 5-hour Energy Drink®, Beaver Buzz®), chocolate, cocoa)

Interaction
Other NSAIDs (e.g., ibuprofen) are sometimes used in combination with caffeine for increased pain relief.

Significance
There is currently no research regarding naproxen/caffeine combinations for this purpose.

Think First
Caffeine can make you more likely to get side effects from naproxen like an upset stomach or heartburn.

Think First
For some medical reasons your doctor may suggest you take naproxen and caffeine together, but taking them together without your doctor knowing may be a risk.

Cannabis/ Hash
(marijuana, mary jane, BC bud, blunt, chronic, J, jay, joint, hemp, pot, grass, herb, 420, dope, THC, weed, reefer, ganja, gangster, skunk, hydro, hash oil, weed oil, hash brownies, grease, boom, honey oil, K2, spice, poppers)

Interaction
a) Marijuana may theoretically increase the risk of bleeding when used with naproxen.
b) Cannabidiol (CBD) and 9-THC may theoretically result in reduced naproxen metabolism and thus increased adverse effects of naproxen (GI upset, GERD, risk of GI ulcer or bleed).

Mechanism
a) 9-THC and cannabidiol may inhibit platelet aggregation.
b) CBD and 9-THC may inhibit CYP2C9, although this has not yet been proven at doses used in human studies. Naproxen is a substrate for CYP2C9.

Significance
a) Caution patients that using marijuana while taking naproxen increases the risk of bleeding.
b) Until more is known about the enzyme inhibition caused by CBD and 9-THC, caution patients that naproxen use with cannabis may increase the risk of adverse effects such as GI upset or bleeding.

Think First
When taking naproxen there is a small risk of you bleeding more than normal. Using cannabis can increase this risk and make it more likely for you to bleed more than you should.

Think First
Cannabis may slow down the removal of naproxen from the body. This might give you more side effects from naproxen like an upset stomach or heartburn.

Cocaine/ Crack
(coke, snow, flake, nose candy, blow, lady white, stardust, rock, crystal, bazooka, moon rock, tar)

Interaction
No information currently available.

Unknown Dangers
Unknown dangers.

Opioids
(codeine, Tylenol #3®, cody, meperidine, Demerol®, DCM, dextromethorphan, roba, skittles, morphine, morph, monkey, methadone, bupe, sub, or dollars, oxycodone, Oxycontin®, hillbilly heroin, OxyNeo®, OC, oxy, roxy, perc, fentanyl, Sublimaze®, Duragesic®, china white, hydrocodone, Hycodan®, Vicodin®, buprenorphine, vika, heroin, H, horses, junk, smack, brown sugar, black tar, down, china white, purple drank, W18, carfentanil, elephant tranquilizer, loperamide, lope, lean)

Interaction
OPIOIDS: Various studies have demonstrated reduced opioid requirements when NSAIDs are given peri- or post-operatively. One systematic review showed a mean 10.2 mg decrease in morphine consumption when patients were on NSAIDs compared to placebo.
However, a study that added acetaminophen/oxycodone to naproxen for low-back pain did not show any improvement in pain compared to naproxen alone.

**MORPHINE:**

- a) In a study of cancer patients who were receiving high-dose morphine, researchers found that patients were more likely to experience myoclonus if the patients were also receiving antidepressants, antipsychotics, or NSAIDs (including naproxen).
- b) There may be an increased risk of respiratory depression when morphine is used with an NSAID.

**TAPENADOL:**

Naproxen 500 mg was given twice daily x 4 doses to 34 healthy subjects. The AUC of a single 80 mg dose of tapentadol (given after the third naproxen dose) increased by 17% but the maximum concentration was unchanged.

**Mechanism**

**OPIOIDS:** NSAIDs are opioid sparing medications.

**MORPHINE:**

b) This interaction occurred with related NSAID diclofenac and morphine, but may generalize to other NSAIDs. It is thought to be a result of the elevated concentrations of morphine-6-glucuronide which remained elevated for several hours.

**Significance**

**OPIOIDS:** NSAIDs may reduce opioid requirements and possibly some opioid-induced adverse effects. However, there is some conflicting evidence about the benefit of adding opioids to NSAIDs.

**MORPHINE:**

b) The significance of these results is not understood and the results have been questioned.

**TAPENADOL:**

Due to the lack of change in maximum concentration, no dose adjustment of tapentadol is required when used with naproxen.

**Think First**

**OPIOIDS:** For some medical reasons, your doctor may prescribe you naproxen and an opioid together. But, using opioids without your doctor knowing is a risk.

**Serious Risk for Harm**

**MORPHINE:** Taking morphine together with naproxen may cause slowed breathing. This can be very dangerous.

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**Amphetamines/ Stimulants**

(uppers, ecstasy, E, X, Molly, mesc, XTC, love drug, MDA, MDE, Eve, MDMA, Adam, discom biscuits, bennies, black beauties, Dewedrine®, Adderall®, dexies, Ritalin®, speed, crystal, ics, glass, crank, tweak, cat, qat, khat, bath salts, ivory Wave, Vanilla Sky, Cloud 9)

**Interaction**

No information currently available.

**Unknown Dangers**

Unknown dangers.

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**Phencyclidine/ Ketamine**

(PCP, angel dust, PeaCe Pill, rocket fuel, love boat, embalming fluid, elephant tranquilizer, hag, illy, wet, wet stick, dipper, toe tag, cadillac, snorts, or surfer, Special K, vitamin K, CVR, cat tranquilizer, cat valium, jet, kit kat, Ketalar®)

**Interaction**

No information currently available.

**Unknown Dangers**

Unknown dangers.

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**LSD/ Hallucinogens**

(acid, blotter, cartoon acid, hit, purple haze, trip, white lightning, raggedy ann, sunshine, window-pane, microdot, boomers, buttons, mesc, peyote, salvia, morning glory seeds, flying saucers, licorice drops, pearly gates, magic mushrooms, shrooms)

**Interaction**

No information currently available.

**Unknown Dangers**

Unknown dangers.
Benzodiazepines
(benzos, downers, tranquilizers, tranks, Ativan®, Halcion®, Klonopin®, Rivotril®, Restoril®, Serax®, Valium®, Xanax®, Rohypnol® (roofies, rope, the forget or date rape pill))

Interaction
a) A double-blind, crossover study found no clinically important changes in mood or attention in subjects given naproxen and diazepam.

b) In a study of 10 healthy participants, who received a single dose of naproxen 500 mg and diazepam 10 mg, investigators found the naproxen peak serum levels decreased by 23%, the time to peak levels increased from 1.36 hours to 2 hours, and the diazepam absorption rate constant was reduced by 40%. No other pharmacokinetic changes were observed. Despite these changes, the investigators concluded that it did not appear that any special precautions were required when naproxen and diazepam were used concurrently.

Significance
b) This study suggests that the effects of naproxen may be diminished in the presence of diazepam. However, this is a very small study so until more data is available no dose adjustment of naproxen is required.

![Unknown Dangers]

Unknown dangers.

References
ALSO SEE IBUPROFEN
e-CPS [Internet]. Canadian Pharmacists Association; 2016. Nonsteroidal Anti-inflammatory Drugs (NSAIDs) [CPhA Monograph]; [updated 2014 Oct; cited 2017 Jul 12].
Therapeutic Research Center. Natural Medicines [Internet]. Somerville (MA): Naproxen; [cited Jul 12, 2017].

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