

Homemade Tonic Syrup So Good It'll Stop Your Heart

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Background

So, you want to make your own tonic syrup. You do a quick google search, grab some cinchona bark, and go to town, right? Not so fast! You want that quinine goodness, but it turns out that's not the only thing hiding out in that bark - like quinidine. Sure, it sounds like quinine, and both can cause cinchonism – nausea, headaches, dizziness, blurred vision, ringing in the ears – miserable stuff but generally wears off and not deadly. The biggest safety difference is that quinidine has far more potent effects on the heart rhythm – potentially fatal ones. Cinchona bark is between 0.25-3% quinidine, so if your recipe calls for 10g of cinchona then you might have up to 300mg of quinidine. So should you care about a few milligrams of quinidine ending up in your drink? Yes. Here's why:

Quinidine Effects

The problem with quinidine is that the arrhythmogenic effects can occur well below therapeutic ranges. Potentially fatal rhythms have been documented in patients with known propensity for arrhythmia (Am Heart J. 1986 Jun;111(6):1088-93), but even in healthy patients low doses can increase the risk as I'll try to explain further. Recognizing it's an oversimplification, the part of the electrical cycle of the heart that is most associated with these types of abnormal rhythms is what we call the QTc, and the longer it is, the higher the risk. Some people have congenitally long QTc, some have a long QTc due to other medication effects, and women tend to have longer QTc on average compared to men. Quinidine lengthens the QTc, but just how much and at what doses?

How strong is the effect?

One study compared the effect on QTc before and after 3mg/kg of quinidine sulfate on 48 healthy volunteers (Br J Clin Pharmacol. 2003;56(2):198). Bearing in mind that the bioavailability of quinidine sulfate can be highly variable (45%-100%), the vast majority had fairly consistent absorption, resulting in a mean and SD maximum concentration at the two hour mark of 871 +/-57 ng/mL in women and 997 +/-56 ng/mL in men (no statistically significant difference). At that maximum serum concentration women and men had QTc prolongation of 33 +/-16ms and 24 +/-17ms, respectively. These patients started with normal QTc (414.8 +/- 22.8ms and 397.9 +/- 18.9ms for women and men, respectively), and with the quinidine effect were still generally within the normal QTc range.

Another study which used a single blinded crossover design in 24 volunteers (Clin Pharmacol Ther. 2000;67(4):413) evaluated the slope of QTc versus serum concentration, and consistent with the above study found that women had a larger effect than men. Please note that these numbers refer to micrograms/mL rather than nanograms/mL in the prior study, but for women and men, respectively, the QTc changed 42.2 +/- 3.4ms versus 29.3 +/- 2.6 ms per microgram per mL. These effects are consistent with the findings of the other study: if one were to use this study's slope and the first study's measured concentration, the predicted QTc change is within a few milliseconds of what that first study measured.

So what's a safe dose?

Like most things in medicine, that depends on a few factors. We divide QTc into ranges of normal, borderline prolonged, and prolonged. The difference between the upper limit of normal for QTc and the upper limit of borderline prolongation is 20ms, so if we assume (my least favorite word in medicine, so we'll come back to it) that our customer/patient has a normal QTc to start with, then a prolongation of 20ms would still not put them into the "prolonged" category where we consider the risk to lie. So how much quinidine would we expect to result in a 20ms prolongation? For that let's calculate a "maximum predicted effect." Recognizing that absorption is highly variable, let's be conservative and use 100% bioavailability. The volume of distribution of quinidine is 2-3L/kg, so using the more conservative 2L/kg, a 1mg/kg dose that is completely absorbed would result in a serum concentration of 0.5 micrograms/mL. Using the studied effects above we would predict the effect on QTc for women (focusing on them since their effect is stronger) of 21.1ms. The effect on QTc in the study using a 3mg/kg dose was only about half as strong as this "maximum predicted effect," but there's something to be said for using conservative estimates when it comes to adverse effects.

Yeah, but how much can I safely put in a drink?

Well, how much does your smallest female customer weigh? What if she has more than one drink? Does that make her the highest risk person in the bar? Not necessarily, because we simply cannot assume that someone has a normal QTc to start with. **On average, one out of every hundred people who walk into the bar will start with a prolonged QTc (not to mention the others starting with a borderline prolonged QTc or happen to be taking other medications that prolong QTc like many antibiotics and psychiatric medications) – and most won't know it. If someone already has a prolonged QTc, then no amount of further prolongation is truly "safe," and I would say they should avoid quinidine altogether.** Does that mean an asterisk for any cocktail containing quinidine? I'll leave that up to you, but stating that "people who are prone to arrhythmia should entirely avoid consuming drinks containing quinidine" is pretty sound medical advice.

So unless your bar has an EKG machine and a doctor to interpret the readout, leave rolling the dice to playing Cee-lo, since most of your customers would never know whether even a small dose could be fatal until it's too late.

(For additional questions, please reach out to me @CocktailMD)