# A formula for better asthma, cold and heart medications

Imagine that you had found a way to drop the dose of your asthma medication ten-fold, increase its duration of activity from a couple of hours to all day, and still get the same relief as before. Imagine that you could use the same approach to improve decongestants, antihistamines and heart medications. What you'd get is less side effects and more and longer relief. Who wouldn't want that!

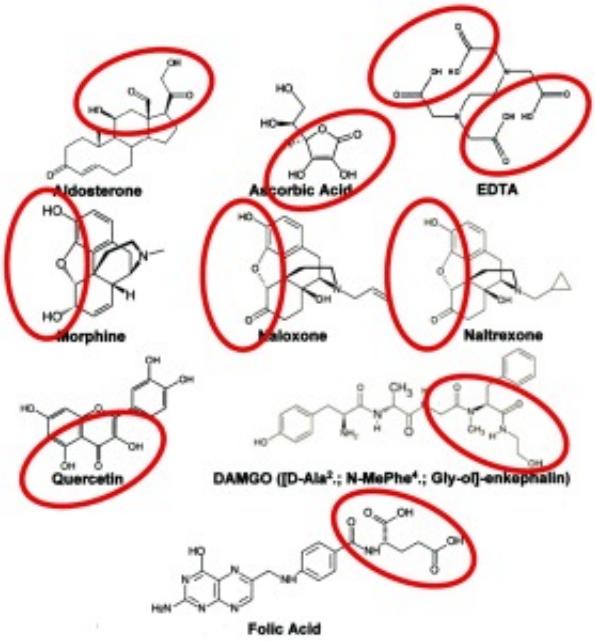


Fig. 1. Aldosterone, ascorbic acid (vitamin C); EDTA (ethylenediaminetetraacetic acid); morphine (an opiate drug), DAMGO (a pharmaceutical variant of naturally occurring enkephalins, which are the body's own opiates); opiate antagonists such as naloxone and naltrexone; quercetin (a plant pigment called a "flavonoid" that is, like vitamin C and EDTA, an antioxidant); and folic acid (a B vitamin) are all known to enhance one or more adrenergic drugs (e.g., epiniphrine or adrenalin). The red circles show that despite the very marked differences in their overall structures, all of these compounds share similar sets of double-bonded O and OH;s in similar configurations. Root-Bernstein and Dillon proposed that these configurations explained how such different compounds could have a common enhancing effect on adrenergic drugs and predicted that any compound sharing the same motif would also act as an enhancer (see Fig. 2).

These effects have already been produced by Robert Root-Bernstein and Patrick F. Dillon, two physiologists at Michigan State University, working with tissue and animal models. Over the past ten years, Root-Bernstein and Dillon, working with several of their colleagues, have demonstrated that vitamin C enhances the effects of epinephrine (sometimes called adrenalin) and similar

compounds used to treat asthma, such as albuterol. Far less drug is required to obtain relief from the bronchoconstriction that causes asthma and even with the decreased drug dose, the duration of that relief is extended by many hours.

Drugs such as epinephrine and albuterol belong to a broader class of drugs called “adrenergics”. Adrenergic drugs make up about a third of all the drugs currently on the market and include decongestants such as those found in Afrin, Sudafed, Mucinex, Claritin and Zyrtec. Root-Bernstein and Dillon have demonstrated that many of these drugs can also be enhanced by the addition of vitamin C. They have shown similar improvement by linking vitamin C directly to a heart drug. And vitamin C also enhances histamines (which cause allergy symptoms) and antihistamines (which block allergy symptoms).

In their most recent studies, Root-Bernstein and Dillon have explored the mechanism by which vitamin C performs its enhancement, looking for a basic principle that might permit pharmaceutical companies to design better-enhanced drugs. One clue came from the fact that several other compounds also enhance adrenergic drugs. These enhancers include opiates, such as morphine, and opiate antagonists (drugs used to treat a morphine over-dose), as well as EDTA, a compound known as a “chelator” that some people use to “cleanse” their blood. Using such clues, Root-Bernstein and Dillon were able to infer a common molecular motif (or structure) common to all known adrenergic enhancers. From this motif, they predicted a new enhancer: tartaric acid.

Tartaric acid is a compound found in many plants, but especially in grapes, grape juice and wine. It is also sometimes used in baking and, like vitamin C, as a food preservative.

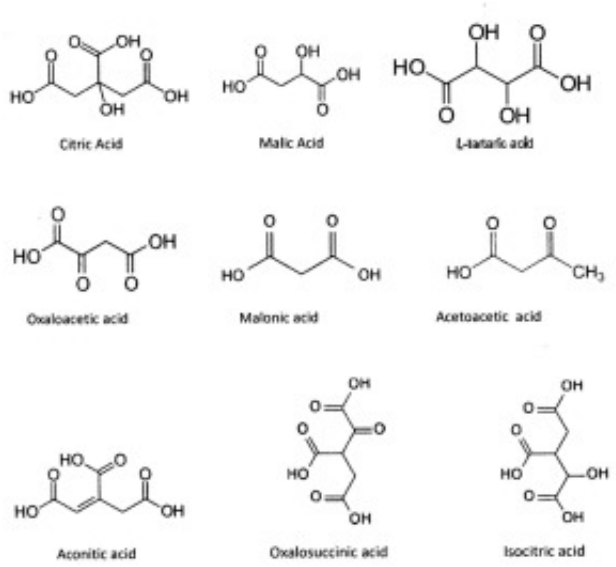


Fig. 2. All of the compounds in this Figure are metabolites used by the body to produce energy and they share the common molecular motif illustrated in Figure 1 and are therefore predicted to be able to enhance adrenergic drugs. Root-Bernstein and Dillon demonstrated that one of these

compounds, tartaric acid, a compound commonly found in grapes and grape products such as wine, does, indeed, enhance adrenergic drugs. Thus, many safe and effective compounds may exist that can be used to improve drug formulations for asthma, colds and heart disease treatments.

In their latest paper, Root-Bernstein and Dillon demonstrated that tartaric acid works as well as vitamin C to enhance epinephrine. They predict that many other compounds that are structurally similar and equally safe exist, providing drug developers a very wide range of possible ways to improve their asthma, cold, allergy and heart drug formulations.

But before you go and start taking vitamin C or drinking grape juice or wine with your asthma medication or decongestant, Root-Bernstein and Dillon have some warnings. First, ingesting vitamin C or grape juice won't generate the concentrations of these compounds required to enhance adrenergic drugs. The body metabolizes or washes them out of your system too quickly. Vitamin C or tartaric acid need to be applied with the drug directly to the tissue you want to relieve. That means inhaling them for asthma or cold relief, and no one has studied the effects of repeated inhalation of high doses of vitamin C or tartaric acid into the nose or lungs. It's possible that you will relieve your asthma or cold symptoms but destroy your sinuses and lungs simultaneously! So don't try this at home! Let the pharmaceutical experts do their studies first!

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## Publications

Tartaric Acid Enhances Adrenergic Receptor Activity: Test of a General Theory of Extracellular Aminergic GPCR Enhancer Discovery.
Root-Bernstein R, Fewins J, Dillon PF
*Curr Drug Discov Technol. 2014*

A common molecular motif characterizes extracellular allosteric enhancers of GPCR aminergic receptors and suggests enhancer mechanism of action.
Root-Bernstein R, Dillon PF
*Curr Med Chem. 2014*

Receptor-mediated enhancement of beta adrenergic drug activity by ascorbate in vitro and in vivo.
Dillon PF, Root-Bernstein R, Robinson NE, Abraham WM, Berney C
*PLoS One. 2010 Dec 13*