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Why you've never heard of the mint versus Covid hypothesis: a philosophical perspective

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Abstract

Recent evidence suggests the intriguing hypothesis that consuming common culinary herbs of the mint family might prevent or treat Covid. Individual citizens could easily explore the hypothesis using ordinary kitchen materials. I offer a philosophical framework to account for the puzzling lack of public health messaging about this interesting idea.

Keywords: COVID-19, Covid19, SARS-CoV-2, pandemic, coronavirus, Lamiaceae, perilla, sage, tea, caffeic acid

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Introduction

Evidence-based medicine has been defined as "the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients" (Sackett et al., 1996). This philosophical approach addresses the problem that human intuition is fallible, even for experienced physicians. An idealized gold standard of medical evidence might consist of large peer-reviewed randomized controlled trials (RCTs) that have been published in reputable journals and confirmed by independent investigators. Laboratory findings and observational studies (in which the health status of individuals who happen to have independently chosen different behaviors is retrospectively analyzed) can also provide useful evidence that generates testable predictions (Dubner, 2022; Lee et al., 2012; Tulchinsky, 2018). The television series *Dopesick* dramatizes the problems that can arise when physicians assign undue evidentiary weight to the opinions of regulatory authorities and product sales representatives (Strong, 2021).

Evidence-based approaches are challenging in situations where the best available evidence is weak or equivocal. The infamous Tuskegee Study of Untreated Syphilis (TSUS) provides a grim illustration of the challenge. Although penicillin had become a standard treatment for primary syphilis by the 1940s, evidence of its utility for treating later stages of the disease was generally considered preliminary and inconclusive. Study organizers chose not to inform TSUS volunteers of the emerging treatment option (Gray, 1998). The decision to passively encourage patients to gamble with untreated syphilis rather than informing them of the newer option of gambling with unproven penicillin appears to have rested, at least in part, on the paternalistic view that the African American study volunteers were too ignorant to make sensible medical decisions for themselves (Sargent, 1997; White, 2019). A similar problem also existed in the contemporaneous society at large. It was standard practice at many major medical centers, including highly respected centers such as Stanford, to deny penicillin to all syphilis patients over age 50, based on the false assumption that the treatment would be unlikely to provide net benefit (White, 2000). The problem is attacked satirically in the "sit tight and assess" scene in the popular movie *Don't Look Up*, where political leaders decide to secretively wait for more conclusive evidence while an extinction-level comet bears down on civilization (McKay, 2021). In short, discounting valid preliminary evidence can lead to withholding of crucial information and the rationalization of "cautious" inaction that fails to avert a predictable calamity. Reliance on strictly proof-based medicine becomes particularly problematic during public health emergencies (Klein, 2021; M. Lewis, 2021).

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In situations where available medical literature doesn't support standard recommendations about how to proceed, physicians, patients, and regulators must resort to using inconclusive lines of evidence to generate rational best bets about the likely risks and possible benefits of various courses of action. The risks and benefits of inaction must also be weighed, but in some cases - such as syphilis infection - watchful waiting obviously isn't the best bet. As Franklin Roosevelt once put it:

> It is common sense to take a method and try it. If it fails, admit it frankly and try another. But above all, try something. The millions who are in want will not stand by silently forever while the things to satisfy their needs are within easy reach (Roosevelt, 1932).

From a patient's perspective, the physician's goal in this challenging situation should be to help the patient understand the various medical options well enough that the patient can rationally choose the path that best fits their own risk/benefit preferences.

Vaccination is a safe and effective way to prevent severe acute Covid, particularly if booster doses are employed (Bar-On et al., 2022). Unfortunately, so-called "mild" Covid can still cause a wide range of serious long-term health problems, even among vaccinated individuals (Al-Aly, 2022; Altmann, 2022; Chertow, 2022; Cohen et al., 2022; Douaud et al., 2022; Edlow et al., 2022; Güthe, 2022; Y. Liu et al., 2021; Martin, 2022; Rutkai et al., 2022; Sansone et al., 2021; Shen et al., 2022; Su et al., 2022; Tapper, 2022; Wang et al., 2022; Xie et al., 2022). Vaccinated individuals are therefore advised to continue to protect themselves and others with high-filtration face masks (Ansberry et al., 2022; Collins, 2021). It would be useful to have additional preventive options.

Although a wide range of traditional herbal remedies have not withstood careful scrutiny in RCTs, there have been a few notable success stories. Teas made from the leaves of various wormwood species (genus *Artemisia*) have been used as fever remedies for thousands of years (Hsu, 2006). Natural product screening efforts and RCTs have established that artemisinin, a compound found in wormwood leaves, is a potent anti-malarial drug. Subsequent efforts have suggested that preparations of whole wormwood leaves could serve as reasonable low-cost anti-malarial treatments, particularly for populations who can't afford pharmaceutical-grade artemisinin (Weathers et al., 2014). In some trials, wormwood leaf-based treatments appeared to be more effective than much higher doses of purified artemisinin. It has been suggested that the use of whole-leaf preparations could help combat artemisinin resistance because the crude mixture contains a range of additional antimalarial compounds alongside artemisinin. Consumption of whole plant products is thus an intriguing approach to fighting infections.

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Humans must eat to survive and eating certain foods is likely to confer health risks or benefits. In an abstract sense, every meal is a poorly controlled mandatory medical experiment resting on inadequate scientific evidence. Based on emerging literature, I hypothesize that eating mint family (Lamiaceae) herbs might reduce the risk of becoming infected with SARS-CoV-2 or might attenuate existing Covid infections. The hypothesis could be tested with randomized controlled clinical trials. While such trials are being developed, I propose that it is reasonable for citizen scientists to consider crudely testing the hypothesis in their home kitchens.

Evidence

The subject of plant products that might inhibit the replication of coronaviruses has recently been reviewed (Bosch-Barrera et al., 2020; Mukherjee et al., 2022; Zrig, 2022). This overview focuses on findings for common culinary herbs of the mint family.

In February 2021, Jan and colleagues published a high-profile peer-reviewed laboratory study testing the ability of traditional herbal and fungal extracts to inhibit the replication of SARS-CoV-2 in culture (Buck, 2021; Jan et al., 2021). Water extracts of the leaves (but not the roots or seeds) of all tested mint-family herbs were found to inhibit SARS-CoV-2 replication at dilutions of at least 64-fold (starting from a 50 gram per liter stock). Administration of water extracts of field mint (*Mentha haplocalyx*, also known as bò hé) or perilla (*Perilla frutescens*, also known as shiso) to SARS-CoV-2-infected hamsters at a dose of 200 mg/kg/day reduced viral loads. If scaled for human body size, the hamster dose would be roughly the equivalent of drinking two cups of mint tea per day, where each cup is made with three standard tea bags.

The SARS-CoV-2 inhibitory effects of perilla in a cell culture model were independently reported in a peer-reviewed study by Tang and colleagues and in a preprint by Le-Trilling and colleagues (Le-Trilling et al., 2020; Tang et al., 2021). An important aspect of the latter study is that it used boiling water for the extraction, suggesting that the hypothetical antiviral compounds are heat-stable. A more recent version of the preprint suggests that the active antiviral compounds may include caffeic acid, perilla aldehyde, and perillyl alcohol, which may exert anti-SARS-CoV-2 effects through induction of heme oxygenase 1 expression. Baicalein, which is found in the mint family herb Baikal skullcap (*Scutellaria baicalensis*), has also been shown to have antiviral effects against SARS-CoV-2 in a mouse challenge model (Huang et al., 2020; H. Liu et al., 2021; Patocka et al., 2021; Song et al., 2021). Interestingly, the antiviral potency of plants tested by Jan and colleagues appears to roughly match each plant's caffeic acid content

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(Birková, 2020). It would be interesting to test yerba mate (*Ilex paraguariensis*) and black chokeberry (*Aronia melanocarpa*), which contain much higher levels of caffeic acid than typical mint-family herbs (Bojic et al., 2013; Shan et al., 2005). Although sunflower seeds contain more moderate amounts of caffeic acid, they could easily be eaten in higher amounts than mint-family herbs.

Two current preprints report RCTs examining candidate Covid therapeutic preparations containing mint-family herbs. Lionis and colleagues found that Covid patients given a mixture of steam-distilled essential oils from three mint-family herbs (conehead thyme (*Thymus capitatus*), Greek sage (*Salvia fruticosa*), and dittany (*Origanum dictamnus*)) suffered less-severe symptoms than the control group (Lionis et al., 2021). A preprint by Faramarzi and colleagues indicates that Covid patients who ate a complex herb mixture including the mint-family herb za'atar thyme (*Zataria multiflora*) showed improved survival (Faramarzi et al., 2021).

Discussion

The current lack of public health messaging about the possible antiviral value of mint-family culinary herbs seems to fit a broader pattern of authorities passively waiting for the accumulation of conclusive proof before addressing an unfolding crisis. Americans under age 50 are currently being denied a second booster dose because some authorities feel the available evidence doesn't conclusively prove the boost is necessary (Salzman, 2022). A different way of looking at the question would be to note that available evidence also doesn't conclusively prove the booster dose is *not* necessary. Indeed, valid preliminary evidence suggests the second dose realistically *might* provide substantial net benefit. History teaches us that, in situations such as this, the safest overall approach may be to openly inform people of scientific uncertainties and then allow us to exercise the basic civil right of making medical decisions for ourselves.

Early-pandemic guidance recommending the use of cloth face masks appears to be another example of the sit tight and assess fallacy. A 2015 RCT conducted by MacIntyre and colleagues provided preliminary evidence that medical masks with a melt-blown inner layer can effectively reduce the risk of respiratory infections in a healthcare setting (MacIntyre et al., 2015). Surprisingly, the trial also found that the use of cloth masks slightly *increased* rates of respiratory infection. More recent RCTs have confirmed that cloth masks conclusively fail to prevent SARS-CoV-2 transmission in a community setting (Abaluck et al., 2022; Ansberry et al., 2022). MacIntyre and colleagues' 2015 inference that "the results caution against the use of cloth masks" seems to have been ignored because authorities judged there to be insufficient proof

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that SARS-CoV-2 is transmitted via cloth-permeable aerosols (Lewis, 2022). With hindsight, it would have been better to advise citizens of valid preliminary evidence suggesting it *might* be better to use medical masks or high-filtration respirators while waiting for more definitive proof on the question of aerosol transmission.

Mint-family herbs are pleasant foods that are inexpensive, widely available, easy to prepare, nutritious, and generally recognized as safe at levels routinely consumed by humans for thousands of years. In my opinion, it would be reasonable for public health agencies to highlight valid preliminary evidence suggesting mint realistically *might* offer medical benefits and to note that individual citizens could reasonably decide to try these foods as a best bet for helping to fend off Covid. Just as there is no guarantee that second booster doses will work, there is no guarantee that mint tea will work. The point is that valid preliminary evidence indicates booster doses and mint tea have a fundamentally better risk/benefit profile than now-disproven approaches such as cloth masks and ivermectin (Abaluck et al., 2022; Lim et al., 2022).

The pandemic has presented tremendous challenges for public health messaging - with disinformation, irrational conspiracy theories, and wishful thinking obscuring crucial guidance. Although political leaders worldwide have vowed to “follow the science,” this often seems to mean withholding recommendations until conclusive peer-reviewed RCTs have been independently confirmed by multiple groups and regulatory bureaucracies have issued final consensus opinions. In other words, public health policy has tended to focus on the more confident final stages of the scientific method, while failing to recognize that the earlier stages of the scientific method are designed to address intellectual *un*certainty. When conclusive best-practices are uncertain, following the science should not mean mandatory inaction - it should mean we carefully weigh *all* valid evidence, openly acknowledge scientific uncertainty (Rothman & Melwani, 2016), and then proceed to experimentally test our best bets.

It is interesting that Covid burden has been relatively low in Thailand and Vietnam, where typical cuisine makes frequent year-round use of mint-family herbs. Similarly, mint tea is a popular beverage throughout the Middle East. Observational surveys could be used to search for correlations between consumption of mint-family herbs (or other foods) and Covid risk (D. Lewis, 2021; Merino et al., 2021). In the longer run, it would be interesting to identify and purify candidate antiviral compounds from common foods, understand their mode of action, subject purified pharmaceutical-grade products to large independently replicated peer-reviewed RCTs, and obtain regulatory authorizations. In the meantime, mint-family herbs are delicious.

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Appendix: Recipe Development

Recipe 1: Iced Tea. Drinking a daily glass of strong iced tea is a pleasant way to achieve a >200 mg/kg/day intake of mint-family herbs. Approximately 50 grams (1⅔ cups) of loose-leaf mint-family herb tea products were mixed with half a liter (one pint) of room-temperature water for an hour. The cool-water extract was poured into a pitcher using a funnel fitted with a mesh strainer and the retained leaves were re-steeped in half a liter of near-boiling water for an hour. The cooled hot-water extract was then strained and combined with the initial cool-water extract. An optional 25 grams of honey (1 tablespoon) or 40 grams (¼ cup) of table sugar per liter balances herbal bitterness without being overly sweet. Excellent iced teas can be produced with the same herb combinations used for hot tea (see below).

Recipe 2: Hot Tea. Hot tea was made by placing 12 grams (¼ cup, five tea bags) of loose-leaf mint-family tea products in an infuser basket (OXO) and steeping in roughly 250 milliliters (1 cup) of near-boiling water for 10 minutes. Some testers preferred to use a French press because it produces a tea with less sediment.

Since it is not certain which mint-family herb varieties might have more or less of the hypothetical antiviral compounds, a bet-hedging strategy of mixing together at least three different mint-family herbs was employed. Testers were encouraged to try different combinations, both out of culinary interest and based on a desire to implement the general nutrition theory that eating a varied diet is healthy. Single-herb commercial products were preferred because appearance and flavor could be used to guard against counterfeiting (Piller, 2022).

All tea mixtures included at least one mint-family herb species with evidence of relatively potent anti-Covid effects. These included (roughly in descending order of aggregate quality of evidence for antiviral effects) field mint, perilla, sage (*Salvia officinalis*), oregano (*Origanum vulgare*), self-heal (*Prunella vulgaris*), catnip (*Nepeta tenuifolia*), and American skullcap (*Scutellaria lateriflora*)(Jan et al., 2021; Le-Trilling et al., 2020). Teas also included at least one pleasant-flavored mint-family herb, including (roughly in descending order of palatability) peppermint (*Mentha x piperita*), spearmint (*Mentha spicata*), lavender blossom (*Lavandula angustifolia*), sacred basil (*Ocimum tenuiflorum*), rosemary (*Salvia rosmarinus*), dittany, lemon balm (*Melissa officinalis*), mountain tea (*Sideritis scardica*), thyme (*Thymus vulgaris*), hyssop (*Hyssopus offininalis*), Greek sage, and patchouli (*Pogostemon cablin*).

A mixture of field mint (Sailing Boat) and powdered perilla (Prince Herb) has an interestingly complex earthy mint flavor. Another palatable mixture consists of one bag

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of Buddha Teas Sage together with three bags of Celestial Seasonings Mint Magic (which contains spearmint, peppermint, and cinnamon). Harts of America Lemon-Lavender-Mint (lavender, lemon balm, peppermint, spearmint) is another pleasant blend. Although it involves somewhat more effort, teas made from fresh herbs (most notably, rosemary) subjected to brief freezing (to rupture cell walls) or ground in a mortar and pestle are excellent.

Oregano was one tester's favorite single-herb hot tea but among other testers' least favorites. The addition of lemon juice and honey was found to balance the bitterness and savory herbal notes of oregano-only tea. All testers but one found teas made with catnip remarkably unpleasant. In contrast, testers generally found lavender tea to be more palatable than expected. In some cases, herbs testers did not enjoy as single-herb teas were found to offer pleasant background complexity in mixed-herb teas. Tea made from purple perilla (Prince Herb) develops a red-plum color when acidified with lemon juice. The effect is attractive in cocktails.

Although fish mint (*Houttuynia cordata*), honeysuckle buds (*Lonicera japonica*), and cassia cinnamon twigs (*Cinnamomum cassia*) are not mint-family herbs, Jan and colleagues observed that they have high antiviral potency in cell culture (Jan et al., 2021). Powdered fish mint (Prince Herb) makes a full-bodied tea with pleasant earthy complexity. Honeysuckle bud tea was judged to be dank and harshly bitter, with no counterbalancing floral or herbal notes. Cinnamon twigs (Plum Dragon) are an excellent adjunct for mint-family teas as well as for brewed coffee. In cases where a caffeinated beverage was desirable, yerba mate (which contains high levels of the proposed active antiviral compound caffeic acid (Bojic et al., 2013; Le-Trilling et al., 2020)) was a pleasant adjunct to mint-family teas.

One tester speculated that single-herb sage tea might be causing headaches after about a week of daily consumption. It is noted that sage contains thujone, which might be hazardous at high doses (Lachenmeier & Uebelacker, 2010).

Recipe 3: Fresh Herbs. During the summer and autumn, daily salads were enhanced with a handful of coarsely chopped mint-family herbs purchased from a local farm market. Herbs were also outdoor container-gardened in Bethesda, Maryland using basement-composted earthworm castings (Worm Factory 360) and automated drip irrigation (Raindrip). Successful species included basil (*Ocimum basilicum*), sacred basil, peppermint, oregano, Vietnamese balm (*Elsholtzia ciliata*), sage, rosemary, hyssop, Korean hyssop (*Agastache rugosa*), spearmint, and Cuban oregano (*Coleus amboinicus*).

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Batches of mixed-herb pesto were made on a roughly weekly basis and applied to various foods throughout the week. At times when SARS-CoV-2 exposure was suspected, a full batch of pesto was served over pasta in a single meal. Traditional pesto recipes call for breaking open plant cell walls using a mortar and pestle. Simpler modern recipes call for pre-softening plant cell walls by briefly blanching the herbs in boiling water prior to chopping in a food processor. To avoid the possibility of losing hypothetical antiviral compounds to the blanching water, cell walls were instead disrupted by freezing the herbs just prior to chopping in a food processor (López-Alt, 2015).

Recipe 4: Other Foods. All tested brands of za'atar, which contains the mint-family herb *Zataria multiflora*, were judged to be palatable sprinkled on bread, salad, or yogurt. Although nigella (*Nigella sativa*) is not a member of the mint family, its seeds have been preliminarily reported to have possible anti-Covid effects in an RCT (Ashraf et al., 2020). Nigella seeds are suitable for all culinary applications where one might use sesame seeds. Dried black chokeberries (Powbab), which contain high levels of the candidate antiviral compound caffeic acid (Birková, 2020), were found to be a pleasant food either eaten whole or ground and brewed as a hot tea. It appears that caffeic acid is stable at roasting temperatures (Mehaya & Mohammad, 2020). Roasted sunflower seeds are an appealing snack food.

The food items were not eaten daily but were instead simply kept on hand as pantry items that could easily be added to the diet in the event that a family member catches Covid.

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