

Opinion

# Insights from selected ancient Mesopotamian medicinal plants: an opinion piece

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## Abstract

This paper is grounded in a series of medical texts that survive from ancient Mesopotamia. It seeks to show the relevance of these texts for the modern researcher. Key findings are that the ancient Mesopotamian physician had already discovered many of the herbal treatments currently being verified by modern science. Armed with what these ancient texts tell us, we are in a position to offer advice on ways to ensure the most effective use of and avoid the dangers presented by selected medicinal plants.

## Background

Ancient Mesopotamians practiced holistic medicine that relied on a combination of ritual and prayer and herbal, animal and mineral medicines [1]. Civilization in what is now Iraq may be traced back to the 4<sup>th</sup> millennium BCE due to a local practice of using clay (and occasionally stone) as a writing medium. Over literally millennia, the available plants were tried and tested to determine what plant or combination of plants was effective for what set of symptoms observed in patients [2]. In the beginning, there were only local plant resources to test for potential medicinal uses. However, trade and occasional conquest made available plants from a variety of ecological zones. In the 2<sup>nd</sup> and later 1<sup>st</sup> millennium, Assyrian expansion more or less permanently brought unprecedentedly vast regions of the Ancient Near East under their control. Assyrians took advantage of the plants that grew in these distant regions and added them to their pharmacopeia, as we shall see.

Although much still remains to be discovered and many of the tablets are damaged or broken, a substantive amount of information on medicinal plants and their uses in medicine is gradually being made available for study by modern scholarship. There survive parts of a 40-tablet series that allowed ancient Mesopotamian physicians to diagnose illnesses, including those that they had no way currently of treating. This is now more or less edited [1] and the difficult task of squaring ancient with modern descriptions of medical conditions has been performed [2] but remains controversial due to a reluctance of too many scholars to believe that

anything so permeated by ritual and prayer could possibly represent rational medicine. The therapeutic texts, which also were organized into a series are slowly and painfully being edited, but mostly with outdated translations of the symptoms the plants are being used to treat. The exception is Scurlock, 2014 [1]. What has yet to be done at all is to collect and organize this information by plant in alphabetical order. I have my own largely unpublished and now outdated listing of plants and their uses, some of which I was able to exploit for Scurlock, 2007, 2020, and 2021 [3-5].

For the plants, there are three more ancient series. The "Nature of Plants" has been ably edited by Henry Stadhouders [6,7]. This gives a description of the plant using an ancient plant taxonomy of the sort that x looks like y; its leaves are like z, etc. We have the plant's name and the most important medical use to which it could be put. There was also a series whose ancient name we do not know but we call *Vademeca*. These, like the Therapeutic Series, remain largely unedited, but once again I have listings by plant use from my own transliterations which will appear in Scurlock, Forthcoming [8]. Finally, there is a 4 tablet series which is known by its ancient name of *Uruanna*. This was a classic herbal handbook that was invented in Assyria in the 2<sup>nd</sup> millennium BCE and which was still a work in progress in the reign of the Assyrian king Assurbanipal (668-627 BCE), who commissioned a new edition in which he took a personal interest. It contained some descriptive material and some notes on habitat and plant use but was primarily

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concerned with allowing the ancient physician to recognize a plant in the drug market by its name in 5 ancient languages, including an early dialect of Aramaic and “Canaanite”, as well as popular names for plants of the “Queen Anne's Lace” and “Dead Man's Fingers” variety. Even more interestingly, it provided a substitution list of plant equivalencies either globally or for specific uses. I am currently editing this text [8] as part of a European Union Project entitled Floriental under the supervision of Robert Hawley. When finished it will include an extensive plant, animal, and mineral index that summarizes all the information contained in the three plant series plus selected samples from the Therapeutic Texts.

What these texts allow us to grasp is the range of plants available to ancient Mesopotamian civilization at its height. We hear of myrrh, which will have been imported from Oman. And from India, imports included useful as well as medicinal plants. For making perfumes, there was *budulhu* (bedellium) [8]. And we also hear of a plant called *kadanu* that is described as a plant that is wool-bearing [8]. That this is our cotton is more than suggested by the fact that the Assyrian king Sennacherib (704-681 BCE) says that he planted them in the palace garden and that they were used to make clothing [9]. And, sure enough, analysis of the royal garments from the Queens' tombs at Kalhu (Nimrud) showed that there were, indeed, some made from cotton [10].

As may be gathered from our survey of the sources, the study of ancient Mesopotamian medicine is still in its infancy. Thus, it is perhaps not surprising that so little that is substantive, synthetic, and untroubled by the magic vs science debate, has actually been produced. And just to add to the difficulties, we are faced with literally hundreds of names of plants that could have grown natively everywhere from Iran, Oman, and India on one side of Iraq to Syria, Egypt, and Anatolia (Turkey) on the other. For the vast majority of these plants, the scientific equivalency is unknown or a matter of debate. Early on, a systematic attempt at plant identification was undertaken by Reginald Campbell Thompson [11] but it is now woefully out of date.

## Prospectus

So why should anyone but Assyriologists care about these texts? It is the purpose of this paper to demonstrate that our ancient ancestors knew quite a bit about plant medicines and that we can benefit from their wisdom. The prospects for achieving this goal are not as bleak as they seem. The Assyrian practice of adopting plants from their subjects under their original names allows for reasonably secure identification of a handful of plants. Where this can be combined with a healthy range of plant uses attested in ancient Mesopotamian texts, it is possible to link up ancient and modern uses for medicinal plants. Where there are enough references to plant use, medical and otherwise, it is even possible to make this alignment without the benefit of etymology.

The methodology to be employed is very simple and straightforward. The first order of business is to collect all the references to the target plants from ancient sources. Next, the ancient indications for use need to be aligned with proper translations of ancient Mesopotamian medical terms to determine how we would diagnose or describe what the plants were supposed to treat. Then these uses need to be researched from PubMed to see whether these uses can be verified as effective on the basis of laboratory experiments, animal testing, and clinical trials.

For two ancient Mesopotamian plants with secure etymologies, namely *šušû*-licorice [5] and *kurkanû*-turmeric [4], I employed this methodology to establish the relevance of ancient Mesopotamian medical practice for the modern physician, lining up properly translated ancient texts, usage by usage, with modern experimentation. In an earlier article, Scurlock, 2007 [3], attempted to identify an unidentified ancient plant (*kamantu*) with its modern equivalent on the basis of plant uses alone, which demonstrated that this is also possible. Future scholars should continue this research for the other ancient Mesopotamian medicinal plants that have secure etymologies, for example, *kamunu* (cumin) and *murru* (myrrh) as well as *sîhu* (Aramaic *šîhâ* equals *Artemesia*). It would also pay to examine plants for which there are numerous references, like *kamantu* and/or that have a particularly striking and unique application, such as *qutratu*-thorn, which was used to treat puerperal fever (N<sub>2c</sub> ii' 13'; A<sub>3+</sub> iii 70) in a woman “whom dirty hands have touched” (BAM 421 i 27'), apparently, like a similar plant, by “creating blood” (AoV v 6; Nd2 ii 13), that is, by bringing down the lochia [8].

And there is much to be gained by making the attempt. Perhaps the ancient Mesopotamian physician found a use for a plant that sounds plausible, but we have yet to try. So, for example, date pits are well known to contain plant estrogens. But would this work in humans as opposed to animals? One ancient Mesopotamian therapeutic treatment uses date pits, charred, ground, wrapped in a tuft of wool in a vaginal suppository for *naæâtu* (irregular bleeding) [1].

Perhaps some ancient Mesopotamian plants could have fewer unwanted side effects than drugs currently in use. Ancient Mesopotamian treatments for the eyes using *kurkanû*-turmeric involve opaque spots and dimmed vision, a condition often associated with eyes full of blood, presumably describing cataracts and retinopathy, respectively [4]. The development of retinopathy (and glaucoma) has been linked to over-activation of N-methyl-D-aspartate (NMDA) which results in cells swelling up (necrosis) and dying (apoptosis) [12]. The modern competitors to curcumin for this condition include actual blockers of NMDA which produces some quite serious side effects: memory impairment, psycho-mimetic effects, and ataxia [12]. Surely, it is worth trying to make a substitution. Indeed, in human trials involving arthritis patients, *Curcuma domestica* managed to hold its own against



ibuprofen and without the latter's side effects of abdominal pain and distension [13].

## Findings

It transpired that, although slow and painful, trial and error armed with a desire to cure or at least alleviate the symptoms of patients rather than confirming some pre-existent theory, viz. humoral theory, produced results that can easily pass modern scrutiny. This is without the benefit of sophisticated laboratory equipment and microscopes that allow modern researchers to fully understand what the plant is doing. It is hardly the case, as we sometimes see it said, that a plant will not work unless the physician knows exactly how it is working its magic. All the ancient Mesopotamian physician needed to know is that it was working and what he could do to make it work better.

As I searched through the thousands of references to my selected plants, I noted that most of the research on plants is being done in India, Iran and the Far East [4]. It was also noticeable that most of the studies involved fractions. Judging from the Mesopotamian evidence, the use of the whole plant and/or its natural parts needs to be more seriously considered. At the very least, it would be useful to go back to the ancient Mesopotamian (Indian, Turkish, Iranian, and Far Eastern) practice of using medicines in combination, either to increase the effectiveness of the “active” ingredient or to mitigate its side effects [5,15-17].

What I also discovered along the way is that plant medicines are real medicines, meaning that they work in sophisticated ways and can harm as well as heal. Take the case of *šušu*-licorice. This is not the American candy of the same name, which is actually made with anise, but the plant (*Glycyrrhiza*) used to make a candy popular in the Netherlands. It is intensely sweet and quite addictive which is a problem since too much of it can actually be fatal [17]. However, in small doses, it has an amazing range of possible medical uses attested already in ancient Mesopotamian texts, as explained in Scurlock, 2021 [5]. That low back pain? Ancient Mesopotamians treated it with *šušu*-licorice in baths and enemas [5]. Were they wise? Not only is *šušu*-licorice good for pain, but modern experimental studies show that licorice promotes sciatic nerve regeneration and functional repair [18].

Ancient Mesopotamian physicians were faced with numerous GI problems, including both enteroinvasive and enterotoxic diarrhea which they also treated using *šušu*-licorice [5]. This will help, but how besides the obvious? A surprising number of bacteria (including *E. coli* and *Campylobacter jejuni*, a major cause of diarrhea) begin by attaching themselves to intestinal epithelial cells. But licorice root contains an anti-adhesive that prevents this, causing them to slide harmlessly down the intestinal wall. The best part of this is that because this therapy is not antibiotic, there is less worry about the bacteria becoming resistant [19].

Even more curious is the way in which *šušu*-licorice deals with the tiny worms that are one of the causes of the urinary-tract problems treated by ancient Mesopotamian physicians [5]. Pity the poor *Schistosoma mansoni* in a patient treated with *šušu*-licorice. These organic egg-laying machines will lay no more eggs. And their essential tegument that does everything from helping them travel about the blood vessels to feeding and repairing injury? Licoflavone B can “massively” disintegrate it [20].

More interesting about the ancient Mesopotamian use of *šušu*-licorice to combat poison [5] is less that it works but just how many poisons it can be used to treat. Experiments have shown that glycyrrhizic acid can lower the toxicity of strychnine, histamine, chloral hydrate, arsenate, snake venom, diphtheria toxin, and tetanus toxin, inter alia. It will also protect the heart against physostigmine and acetylcholine [21]. Perhaps more prosaically, it has been shown to protect both mice [22] and men [16] from developing alcoholic fatty liver.

Ancient Mesopotamian texts prescribe *šušu*-licorice in bandages and baths for arthritis and rheumatism, including “trembling”, presumably Sydenham's chorea [5]. Here, it is less interesting that it works than how it works. It transpires that these preparations help protect the joints by decreasing the levels of two proinflammatory, bone and cartilage destroying, cytokines. It does this by discouraging the spleen from producing them and, what is more, licorice prevented associated oxidative damage to the laboratory mice's liver and kidney tissues [23]. It is also known that glycyrrhizin inhibits HMGB1, a notorious inflammation inducer now implicated in the development of rheumatoid arthritis [24]. Unsurprisingly, ulcerative colitis, another condition that ancient Mesopotamian physicians used *šušu*-licorice to treat [5] also benefits from the inhibition of HMGB1, which is implicated in the increased production of pro-inflammatory cytokines that play critical roles in the pathogenesis of colitis [25].

For epileptic seizures, ancient Mesopotamian physicians supplied amulets containing *šušu*-licorice, handy carry-along treatments worn around the patient's neck, ready to be broken open and used as a potion or salve at a moment's notice [5]. Modern experimental studies indicate that the ethanol extract of *G. glabra* root can delay the onset of clonic convulsion and reduce its duration with results comparable to diazepam, if in much larger doses [26].

Once again, the plant's ability to inhibit the High-Mobility Group Box 1 (HMGB1), which is “massively” released from damaged neurons after an epileptic seizure and contributes to the etiopathogenesis of future seizures by increasing neuronal excitement, comes into play. Glycyrrhizin not only binds HMGB1 but also suppresses neuronal death due to excitotoxicity [27].

And, yet again, the same binding activity of HMGB1 and





suppression of excitotoxicity make it a good choice for the treatment of strokes, yet another use of the plant by ancient Mesopotamian physicians [5]. Experiments show its potential for preventing reperfusion injury, even in some cases, preventing the infarct [28]. Glycyrrhetic acid might even be able to prevent the affected patient from having further strokes [29].

Last but by no means, the ancient Mesopotamian physician used *šušu*-licorice to treat endocrine disorders, probably Addison's disease and almost certainly Graves' disease [5]. The ability of licorice to treat mild or moderate cases of Addison's disease has long been recognized [21,30]. And then there was a woman with Addison's disease who managed to stay alive and well for four years by inadvertently self-medicating with European licorice sticks and "Dragon" soy sauce [31].

The evidence for the effectiveness of *šušu*-licorice in treating hyperthyroidism can be confirmed in a rather backward way by ancient Mesopotamian evidence. Successful treatments for hyperthyroidism carry a significant risk of inducing hypothyroidism, a problem described with pinpoint accuracy in ancient Mesopotamian texts. They even seem to have realized that something in the sour milk they used to decoct the medicines used to treat Grave's disease was causing their patients' symptoms [1].

The situation with *kurkanû*-turmeric is even more interesting. It is homeopathic, meaning that in large doses it will actually cause the symptoms that in small doses it can be used effectively to treat. The key here is dosage; as we see again and again with this plant, nothing happens with a really low dose of curcumin. As the dosage is increased, the expected effect appears and rises to a maximum. After that, no further improvement is experienced until a high dose threshold is crossed, after which the plant actually reverses course and enables what it had been blocking and vice versa [4].

It is this feature that makes it an ideal treatment for wounds, which require, at the beginning, acute inflammation to clean up all that is in the wound that shouldn't be there, like spilled blood, foreign tissue, and bacteria [32]. Once that is done, successful healing requires a urokinase Plasminogen Activator (uPA) which is, in turn, regulated by two of the MAPK signal pathways (JNK and p38) that are favorite targets for upregulation or inhibition by curcumin, the fraction of turmeric that makes it yellow [33]. Last, but by no means least, curcumin stimulates the maturation and cross-linking of collagen, thus accelerating the rate of wound contraction [33,34]. In short, curcumin can handle it all from beginning to end, as the ancient Mesopotamian physician knew [4], even if he didn't know exactly how.

But turmeric is also useful for a wide variety of treatments attested already in ancient Mesopotamia at both ends of its spectrum. So, for ear infections, ancient physicians employed bandages, fumigants, and tampons containing *kurkanû*-

turmeric [4]. Mostly, these are cases of otitis media, a condition caused by the overproduction of mucus produced to entrap pathogens for mucociliary clearance [35]. *In vitro* and *in vivo* experimentation showed that curcumin in low doses was able to down-regulate mucus production which had been put into overdrive by an invading pathogen. Curcumin accomplishes this by deactivating pro-inflammatory p38MAPK pathways by up-regulating protein MAP Kinase Phosphatase-1 (MKP-1) [35]. Interestingly, the ancient physician was aware of this effect. In Uruanna, *kurkanû*-turmeric is specifically recommended as a plant for opening/closing the nose (nR<sub>2a</sub> i 10) and stopping phlegm (from flowing) (nR<sub>2a</sub> i 4) [8].

Usually, it is the anti-inflammatory, antioxidant, properties of low doses of turmeric that are desired [4] but this is not always the case. At the pro-inflammatory, pro-oxidative, high dosage end, will have been used by the ancient Mesopotamian physician of *kurkanû*-turmeric to treat jaundice [4]. This will have worked by removing excess anti-oxidant bilirubin from the bloodstream. Indeed, a clinical trial of liver cirrhosis patients revealed a significant decrease in serum levels of bilirubin after three months of treatment in the curcumin group [36].

So turmeric is dose-dependent, and that is by body weight. Assyrian therapeutic texts never give the dosage for an individual patient, leaving this detail to the expertise of the orally trained physician. Already we in the modern age are in trouble. If we are going to mass produce a drug, we would want a one size fits, not a different drug for every possible body weight. And with every American woman not only changing weight once a month but also on a diet, this could only be practical if the dosage was made up for each individual patient. The saving grace is that the human digestive system takes out most of the effectiveness of turmeric [13]. Therefore, giving it by mouth would save us from potential disaster, if severely limiting what the plant can do for us.

Avoiding the problem of severely reduced effectiveness by making artificial nanoparticles (made from gold, silver, and polymer) out of the active ingredient of turmeric is, however, in my view, extremely ill-advised and unnecessary. Those artificial versions are pleasingly perfect. They are, however, hardly biodegradable. By contrast, the comparatively eco-friendly oil-encased carbon nanoparticles are the hot new super high-tech equivalent of just mixing ground turmeric in oil or ghee before application through the skin as ancient Mesopotamians did. The liposomes are somewhat irregular spheroids and ovoids that vary in size [37] but work just as well as their prettier sisters.

Better yet if the entire plant or plant part is used, as in ancient Mesopotamia, since the essential oil, the terpenes in turmeric, have the capacity to make whatever accompanies them pass more easily through the skin [38]. And that is not all that they do. Whereas curcumin is very useful in treating



cataracts, retinopathy as well as peripheral neuropathies of diabetes, it is the sesquiterpenes that deliver the bulk of the hypoglycemic punch, treating the underlying cause and not just the symptoms produced [39,40].

It can also help to use several medicinal plants together. For example, the ancient Mesopotamian physician used a combination of *kurkanû*-turmeric and “Dilmun dates” = Tamar Hindi in Arabic = *Tamarindus indica* to treat what is clearly reactive arthritis [4]. Studies have shown that these two plants do, in fact, synergize to alleviate pain and improve knee joint mobility [41].

A much-maligned ancient Mesopotamian delivery system that merits revival is fumigation. Burning turmeric and oil, as in ancient Mesopotamia, gives us natural carbon nanoparticles that pass easily through the nasal passages. This delivery method is more effective even than injection [42], yielding almost instantaneous drainage of mucus [43]. Ancient Mesopotamian physicians used this technique to deliver *kurkanû*-turmeric to patients having difficulty breathing [4]. This would have made an interesting alternative to the respirators used to clear the lungs of patients with COVID-19.

And that is not the only reason that turmeric would be a promising treatment for the next viral pandemic. Studies have shown turmeric to be an efficient killer of Y79 retinoblastoma cells. It does this by up-regulating 903 genes and down-regulating 1,319 others, thus doing genetic damage comparable to that of radiation [44]. But that is not all that it does. It also immobilizes them in place and closes cell membranes to their knock, thus helping to prevent metastases [45]. And how does our plant do all this to those Y79 cells? By up-regulating the very pathways (JNK and p38 MAPK) and nuclear factor *NF-kappaB* that it down-regulates when producing its anti-inflammatory effects. For this, we need a high dose of curcumin [46].

Unsurprisingly, turmeric at high doses are also effective against viruses, a use attested for *kurkanû* in ancient Mesopotamian texts in which the plant is used in bandages and fumigants for viral exanthems [4]. Manipulating genetic makeup and preventing pathogens from moving to and entering their victims are particularly devastating to viruses since they do not reproduce by themselves. Instead, virions attach themselves to body cells, which they invade. Next, they hijack the cell's transcription and proliferation systems so that the victim reproduces the virus (vRNA) rather than itself. Once the damage is done, the virions detach themselves and move on to new victims [47]. Turmeric does its helpful work as usual by manipulating the body's own defense systems, up-regulating what the virus has been suppressing, and down-regulating what the virus has been up-regulating to its own advantage [48].

A word of caution is in order. We need to lose the excitement of battle in our treatment of disease, producing

ever more powerful, patentable, genetically-modified versions of curcumin that promise to join a series of other designer drugs whose display of Jekyll and Hyde personality reveals to be similarly homeopathic and dose-dependent [4], a feature which, if properly explored, might help to avoid future disasters. In general, it is preferable to follow the lead of ancient Mesopotamians in favoring gentle treatments that solve the problem without harming the patient even if they do not produce immediate or spectacular results [4] as with the ancient Mesopotamian treatment of uterine atony with *šušulicorice* [5]. *G. glabra* is a complex of flavonoid components some of which agonize and some of which antagonize estrogen, thus making it a selective estrogen receptor modulator [49], and also one for progesterone [50].

## Conclusion

What we have learned so far is that despite the presence of ritual and prayer as well as amulets, the medicine that ancient Mesopotamian physicians practiced was comparable to our own in its philosophy of “use whatever works”. The studies we have been examining highlight just how amazing plants are. They do not do everything nor are they harmless, but what they do they do in sophisticated ways that we are just beginning to understand. And it is exciting to see ancient Mesopotamian physicians taking full advantage of this fact. We should seriously consider taking their lead in using whole plants or plant parts rather than isolated fractions, using combinations of plants rather than producing a single pill that is mostly composed of allegedly inert ingredients, paying way more attention to dosages, and being more open to less common delivery systems including transdermal medication and fumigation. Last, but by no means least, we need to stop demanding immediate and spectacular results and be satisfied with treatments that work at a less frantic pace. In short, what we learn from our Ancient Mesopotamian ancestors is that, if plants are treated with respect, they promise a whole new world that heals without destroying the environment. It may not be as exciting as genetic engineering, but it is more humane and it recognizes the fact that humans are part of the natural world and should not be at war with it.

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