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What's in the Cauldron: Witches, Folk Remedies, and their Contributions to Modern Medicine

Mason Tate Bennett, BS¹

Trinity School of Medicine, St. Vincent and the Grenadines

Correspondence should be addressed to M.B. (mason.bennett.21@trinitysom.net)

Disease is a part of the human condition and before the rigor of the scientific process and peer review, healers had to work with anecdotal folk remedies and word of mouth medicines. These folk remedies were often known by women and shaman who, throughout time, passed on their esoteric knowledge. Some of these remedies, like excretions from toads, Hemlock, Yew, and Foxglove have persisted for centuries and were used for a wide range of ailments. In modern days, with the use of the scientific process and peer review, these plants form the foundation of many medications. This demonstrates the benefit that can be gained with the investigation of folk medicine.

INTRODUCTION

In the fourth act of Macbeth, the Bard introduces us to the Weyward Sisters (1). These sisters

established the stereotypical image of a witch. In the play, before the witches even have a chance to speak, Shakespeare sets them up with a prop. The sisters

were to be in “a cave. In the middle, a boiling cauldron.” It is the contents of that cauldron that are the subject of our investigation.

These witches mix a peculiar concoction, poison excretions of a toad, root of hemlock, slips of yew, and other unsavory items. For what purpose are they creating this potion? It is surely for some evil design, yet, in literature, witches are also shown making medicines and healing salves. Some of the ingredients in the Weyward Sister’s brew are used in modern medicines (2). In Shakespeare’s time, before medical schools and licensed physicians, women labeled as “witches” often had knowledge of the healing arts. There is benefit to be gained by investigating and studying these folk medicines with rigorous scientific inquiry

TOAD SWELTERED VENOM

The Wayward Sisters threw a toad, chosen for its particularly poisonous secretions, into their potion. Oddly enough, practices mirroring this exist today. The Giant Monkey Frog, *Phyllomedusa bicolor*, is found in rainforests of South America. It produces a whitish secretion from its skin, called Kambo, which is used in a shaman ritual of the same name (3). In this traditional healing ritual, a shaman burns a patient with a sharp stick and then applies the Kambo to the lesions (4). Kambo isn’t restricted to tribal shamans. It is occasionally used in Brazil at clinics run by “holistic and medical therapists” (3). These therapists and their patients have reported incredible benefits from Kambo. Claiming that it heals headaches, gastritis, diabetes, depression, epilepsy, cirrhosis, cancer, and AIDS. The National Sanitary Surveillance Agency of Brazil, as well as other academic scientific institutions have not found any evidence to validate these claims (3), and any benefits from the treatment are ascribed to a placebo effect (5).

Most scientific examination has shown Kambo to be dangerous. The amphibious secretions contain bioactive peptides which cause predators to feel nauseated and regurgitate the frogs. These peptides contain excitatory and opiate-like neuropeptides which cause effects such as tachycardia, dizziness, nausea, and vomiting (3). Hypotensive effects

have also been observed which have led to cardiac arrhythmia and sudden death (6). Despite the claims of holistic medical practitioners and its generational use by shamans, it seems that Kambo is not an effective or safe medical therapy. Researchers do suggest that the secretions of the *Phyllomedusa* species could be used for anti-microbial drugs, however, further research and testing is required (3).

Although Kambo has no medical benefit, the idea of using secretions from amphibians has yielded beneficial medical applications, but only once such applications have been thoroughly vetted through academic research. In South America some poison-dark frogs of the family *Dendrobatidae* have secretions containing alkaloids that work as a nicotinic acetylcholine receptor inhibitor. Researchers have tested these secretions to help treat movement disorders, seizures, or autosomal dominant nocturnal frontal lobe epilepsy (7). Other researchers have discovered toxins that act as protease inhibitors (8) which they propose could manage HIV, hepatitis, and even some cancers.

Toads from the genus *Bufo* produce protective secretions that contain alkaloids, steroids, and bufadienolides. The main reason for the secretions is a defense against predators, however, these secretions also protect the toads against pathological microorganisms in their wet environments. This helps insulate the toads against disease as they dwell in habitats where other creatures would fall sick (9). Studies have shown the secretions to have diverse antimicrobial effects against *Staphylococcus aureus*, *Escherichia coli*, and other gram-negative and gram-positive bacteria (10). Anti-viral effects are seen in some of these secretions, most notably from the *Bufo andrewsi* in Asia. Secretions from this toad even inhibit recombinant HIV reverse transcriptase (11). The potential for toad secretions in medicine is staggering since the toxins differ slightly between species leaving many potential medicines to be discovered. Some researchers point out the lamentable fact that the habitats of these toads are being destroyed, thus robbing humanity of a potential solution to diseases that are becoming ever increasingly resistant to established treatments (9).

These amphibious secretions may have seemed demonic and strange back in Shakespeare's day. However, their benefits, when used properly, have been demonstrated by modern scientific inquiry.

ROOT OF HEMLOCK

Hemlock, or *Conium maculatum* (12), is a flowering plant that works on the nervous system, often resulting in death. Hemlock's most famous use is in the concoction Socrates self-administered for his execution (13). This plant is found to contain alkaloids, flavonoids, coumarins, polyacetylenes, and other bioactive compounds (14). At doses higher than 10–20 mg/kg Hemlock is deadly, and its toxicity follows a serious course of symptoms. Starting with weakness in the lower extremities which slowly progresses to the upper extremities, and eventual death by asphyxiation due to paralysis of the diaphragm. Other symptoms include fixed pupils, weak pulse, salivation, loss of urinary control, and nausea (14). Victims remain conscious during most of this, as displayed in the death of Socrates who, after ingesting hemlock, taught the onlooking crowd until he could no longer breathe and died (Brickhouse and Smith).

Doses lower than 10 mg/kg have shown beneficial pharmacological effects. In ancient Greece and Arabia, it was used as an anesthetic and for spasmodic disorders (14). Some, lesser scientific and outdated homeopathic studies are still being cited which propose Hemlock as a treatment for breathing problems, teething in babies, anxiety, Parkinson's, and more (15). This is terrifying and dangerous advice because of the deadly nature of Hemlock.

Stricter, more recent research has attempted to find pharmacologic value despite the danger Hemlock poses. It has been evaluated in rats as a potential medication for pain and nervousness. The researchers compared it against morphine and indomethacin, but it wasn't found to be any more efficacious than existing drugs. Because of this and its narrow therapeutic index, it was deemed inferior to existing analgesics (16).

Hemlock is a teratogen and studies of hemlock ingestion in maternal pigs showed an increase in cleft palates in the offspring (17). Additional

studies of farm animals display other effects of Hemlock's teratogenicity. Goats showed cleft palates as well as spinal deformations. Calves had gross skeletal malformations. Chicks and infant rats had deformities of their toes. All these creatures showed decreased fetal movements in utero (14). Because of its deleterious effects on fetal growth and movement Hemlock was used, along with other herbs, as an abortifacient during the 19th century (18). Due to its unimpressive efficacy, along with its dangerous nature, it isn't recommended as a modern medical treatment. Nobody should ingest hemlock for purposes medical or otherwise.

SLIPS OF YEW

Yew is a plant of the genus *Taxus*. The trees can grow 80 feet tall and their wood is hard and fine-grained. This wood was often used for longbows, as popularized by Robin Hood (19). The bark and the leaves contain bioactive substances including cardiotoxic taxine alkaloids which are calcium channel antagonists. Ingestion of small doses usually causes gastrointestinal discomfort and even vomiting. High doses can cause cardiac side effects such as ventricular conduction problems with subsequent arrhythmia, with one documented case eventually progressing to irreversible cardiogenic shock and eventually death (20). It should be noted that this kind of fatal poisoning is rare. This case happened in 1987 and the woman ingested 150 yew leaves (21). Most people don't go around eating any tree leaves, let alone 150.

In 1960 the National Cancer Institute, or NCI, hired botanists in the United States Department of Agriculture to submit plant samples that were screened for cytotoxicity. In 1962, Arthur S. Barclay submitted a sample of 200 different plants, one of which was a slip of bark from the Pacific Yew Tree or *Taxus brevifolia*. In 1964, the NCI found that extracts of yew bark could kill cancer cells. They had found what they were searching for, a natural source of cytotoxic material (22). They began isolating the cytotoxic compound from these *Taxus* trees and in 1971 the drug, Taxol, was developed, which showed moderate efficacy against tumors (23).

Over time Taxol was shown to be most effective against ovarian and breast tumors and is a standard of care today. Taxol works by inhibiting progression from the metaphase stage of cell division. As microtubules develop, the energy from GTP hydrolysis compacts the alpha and beta subunits of the tubulin complex that makes up the microtubules. This compaction builds tension so that once the microtubule stops growing it will depolymerize. This depolymerization is necessary when the cell needs to breakdown mitotic spindles and progress to anaphase (24). Taxol effectively cancels the impact of GTP hydrolysis by preventing the compaction of the alpha and beta subunits. Without this compaction there is no tension and the microtubules are unable to depolymerize, thus freezing the cell in metaphase. When the cell progression halts it eventually reverts to G₀ phase or apoptosis effectively silencing or killing the cancerous cells (25).

While Taxol is highly effective in its treatment, problems arose with production. The main concern was the environmental impact of harvesting enough bark needed to treat the abundance of cancer in the United States. Roughly 60 pounds of yew tree bark is needed to produce enough Taxol to treat the average cancer patient. The average yew tree produces 12.5 pounds of bark a year (26). Therefore, about 4.8 trees are required to treat one person. This highlights the moral dilemma of creating life-saving drugs at the expense of whole forests of yew trees. In 1990 the Pacific Yew Tree was declared endangered and in 1992 the Pacific Yew Act was passed, protecting trees from being over-harvested (27). Luckily, a breakthrough came in 1993 when a pathway to create synthetic Taxol was discovered (28), and one year later synthesis of Taxol from other plants was also discovered (23).

It is interesting to note that out of all the plant samples obtained by the NCI only the yew tree provided what they were looking for, a cytotoxic compound (22). One must wonder what other possible medicinal properties exist in the hundreds of samples harvested from different plants. If one were to test for other properties beyond cytotoxicity what else could be discovered? Further research should be

done with preference given to plants that have anecdotal medical benefits.

FOXGLOVE

Digitalis lanata, or Foxglove, is a beautiful flowering plant that has a multitude of names; Fairy Caps, Fairy Thimbles, Dead Man's Bells, and Witches Gloves. While Foxglove wasn't mentioned by the Weyward Sisters as part of their concoction, the story of its discovery warrants it a place in this discussion. In 1775 a physician named Dr. William Withering was looking for a treatment for "dropsy", now called edema. Dr. Withering heard of a cure for dropsy that "had long been kept secret by an old woman in Shropshire, who had sometimes made cures after the more regular practitioners had failed" (29).

Dr. Withering interviewed the woman and observed the effects of her medicine. He noted that it provided the desired diuretic effect, along with occasional adverse symptoms of extreme vomiting. Dr. Withering studied the potion, which was made of about 20 different herbs, and was able to pinpoint the diuretic down to Foxglove which he began administering to his patients. After 10 years of experimentation Dr. Withering published the results and proper usage of Foxglove and it was accepted into medical practice (29).

In 1930 British physician Dr. Sidney Smith isolated Digoxin from the Foxglove leaves and demonstrated its impact on the body, not as a diuretic, but by increasing cardiac myocyte contractility (30). Two years later it was accepted for regulated distribution in the medical field and it remains a viable option for treating variable heart conditions (31). Digoxin is a cardiotonic glycoside that increases myocardial force of contraction by reversibly inhibiting the Na-K ATPase pump. It can be used for rate control in atrial arrhythmia by slowing conduction through the atrioventricular node. Its more common use is for systolic heart failure; however, it should be noted that while Digoxin is used to treat heart failure it does not decrease mortality (32).

While the use of Digoxin has begun to wane in favor of safer, more effective drugs, it was an especially useful method of treatment for many years

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CONCLUSION

In Many medical advancements can be made by examining what is “in the cauldron”. Witches and shaman, with their concoctions and folk remedies, have treated illness and ailments for thousands of years. The historical concoctions created in their cauldrons have greatly influenced the modern medical field. From the disgusting excretions of

amphibians, roots of the Hemlock, bark of the Yew, and beautiful petals of Foxglove, we have taken what once seen as sorcery and turned it into medicine. Some of these remedies went thousands of years without an understanding of how they worked, only that they worked. Without the “witches” who used them, we may have never known or discovered their usefulness.

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