

Short Communication

Preparation of drugs in the developing world

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Abstract

The use of non-traditional medicine is routine in certain parts of the world including Africa and South America. These medicines are prepared by health care providers who are often not trained in the western sense, but who provide essential patient services in the more remote regions of these continents. In addition to being able to diagnose and treat disease, these individuals can prepare medicines from their botanical origins. This paper discusses methodology of how to prepare some of these drugs and their use.

Introduction

Access to native, or non-traditional medicines are essential for the treatment of patients in developing countries where health clinics are not readily available [1-3]. Often in the more remote areas medicines are produced by individuals who have no formal training, but are mentored and essentially field trained to not only provide patient treatment, but to manufacture the drugs that are proscribed [4,5]. These people are essential for the health of local populations who may be too far from an urban area, or who may wish to go to local providers for other reasons than location. However, use in the urban areas is increasing [2]. These practitioners provide treatments using procedures that may have been passed down from parent to offspring. Often these medicines are used to treat skin surface bacterial infections or stomach disorders [6]. However, there is some effort to use traditional medicines to treat more complex syndromes such as opportunistic infections associated with AIDS [7].

The treatment of bacterial infections is in the most general sense somewhat straightforward. Bacteria are single cell organisms that are free living in nature. They are comprised of vegetative cellular material that contain protein, nucleic acid, lipid and water. Some species of bacteria contain a spore or endospore which acts much like a seed and allows the organism (and thus the culture) to survive adverse conditions, such as extremes in heat or cold and desiccation. Vegetative cells, protein and sub-cellular organelles are destroyed under these conditions. In this way, the preparation of medicaments are both prepared and reduced in bioburden, in one step.

Product preparation

Until the last 50 years medicines were extracted from plants with a combination of grinding and/or mincing of the dried plant material, followed by boiling in water or simply drying for a period of time. The "extract" was often allowed to concentrate either by continued boiling or by boiling followed by simple (air) evaporation [2,3]. This basic process is used in various parts of the developing world to make human use products to treat patients especially with skin and intestinal disorders [3,6]. The process of medicinal preparation begins with the correct collection of the foliage. Usually this process involves the practitioner identifying the proper plant, and then using the proper portion of the plant as the starting raw material [3,7]. The material is air dried, or in

some cases subjected to mild heat, such as in a low temperature oven, or more basically dried in the sun, and then ground up. It may be dried further in this ground up state or placed in water and boiled. Boiling water treatment will release the active pharmaceutical agent (API) into solution, and away from the remaining plant material [8]. By simple separation of the drug from the plant material an effective raw material is produced. This raw material in the form of an API is then used as treatment. Boiling water has been used to extract nucleic acid and other organelles from bacteria in preparation for further downstream processing, often for genetic analysis in the developed world. This action completely destroys the vegetative elements of both prokaryotic and eukaryotic cells [8]. The boiling action disrupts cellular membranes and the organelles that encompass the living cell.

More recently, the use of organic solvents to increase the efficiency of the manufacturing process is becoming more common, especially in the urban areas where access to these more sophisticated reagents is available to prepare non-traditional medicines. These solvents are more efficient in extracting the API, and also in destroying contaminating bacterial endospores, which are more resistant to chemical and environmental stress. Some of the most used solvents are acetone, methanol and ethanol [1,5,6]. They are inexpensive and readily available. Sometimes the organic solvent is heated, and other times it is not. As an example, while citations concerning the anti-bacterial effects of boiling acetone have not received a concerted experimental effort to determine the actual treatment capability, the effects of ambient acetone treatment on vegetative cells and spores is understood [5,7]. These lessons are essential in many parts of the world that do not have even the most rudimentary laboratory or manufacturing facilities and medicines must be made on-site, "in the wild". From a manufacturing sense the desiccation and boiling serve two functions. The first is

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medicinal extraction, the second is ensuring that the bioburden load is at such a level as to cause no harm to the patient. This is critical as there is no formal quality control of the medicinal preparations.

Anti-microbial effects

The broad spectrum anti-microbial effects of organic solvent derived medicines have been shown by a variety of authors, including individuals who developed the early microbial staining techniques, and has been demonstrated by researchers following different lines of research [1,3,5]. This includes work with fungi and spore forming bacteria. Adedapo and co-workers demonstrated that acetone and methanol extracts of *Bidens pilosa* would kill Gram positive and Gram negative bacteria, including spores from *Bacillus cereus* [4]. Okmen obtained similar results when acetone extracts of *Liquidambar orientalis* was evaluated against several bacterial species including *Bacillus subtilis* and *Candida albicans* [5]. Acetone and alcohols extracts from *Combretum molle* were found to be an effective anti-bacterial agent against drug resistant strains of *Helicobacter pylori*, which is associated with several gastrointestinal pathologies including ulcers [6]. What is not clear sometimes is whether the anti-microbial effect is due to the solvent or the plant derived API. This is true for all the organic solvents that may be used to extract API from plant material. The API and organic solvent may co-exist (undetected) in the same preparation. This is because the citations are unclear as to post-production removal of organic solvents when they are used. In the more remote areas this may not be possible.

Additionally, Otang and co-workers, have shown that acetone extracts of *Arctotis arctotoides* will destroy opportunistic infections associated with HIV [7]. Tanih have shown that acetone extracts of *Sclerocarya birrea* have apoptotic activity against the human breast cancer cell line MCF-7 [8,9]. Similar anti-microbial results were obtained with boiling organics such as Triton X-100 and chloroform in a broad spectrum of Gram Positive and Gram Negative cells, including Mycobacterium [10]. This process is used in laboratories around the world for the extraction of nucleic acids prior to sequencing.

The prospect that bacteria (including spore-forming bacteria) will survive a high heat or boiling solution of acetone and alcohols is unlikely given the available literature. The literature clearly indicate that acetone at ambient temperature is anti-microbial. The effects of the chemical along with the application of heat would cause cell disruption soon after the temperature was raised. This includes deleterious effects on spore forming organisms.

Should any bacteria, bacterial by-product or spore be present at the time of this step in the procedure they should be de-activated or destroyed. The resulting compound should be free of any bacterial contamination. The API should be free of any toxins that may be produced by the reported contaminating bacteria.

Conclusion

The preparation and use of non-traditional medicines will continue in the developing world as it has in the past. The manufacturing, preparation and use of these methods may be passed down and taught to individuals who then take over as on-site care givers for the current generation. This involves a knowledge of both the diseases, disease treatments and the processes for making the drug used [1,2]. The remedies have a higher than expected success rate and are relatively inexpensive to produce, even with the use of more expensive organic solvents. What is somewhat new is the combination of traditional and non-traditional therapy to treat diseases [2]. Despite the efforts of

dedicated individuals to sort out the effects of the synthetic extraction reagent as compared to the actual plant API, little work has been done to define this. In the developing world this issue takes a secondary role to the availability of the preparation to treat the disease. Since most of the organic solvents have an evaporation point lower than water, the chemical will often disipate with mild temperature over time.

Regardless, recent articles have shown the use of non-traditional medicines is on the rise even in urban areas [2]. *Lawsonia inermis* which has long been used as a non-traditional medicine have been screened as an anti-fungal agent [11]. This Algerian plant was extracted with several organic molecules and showed that the presence of lawsone in the leaves was necessary for anti-fungal activity. This was best shown with the ethanol extracts [11]. Extracts of *Calligonum comosum* which have been previously used to treat bacterial infections have been evaluated *in vitro* as an anti-Listerial agent [12]. Western style research continues on the topic of non-traditional medicines and their preparation and use. This is essential in a world which is exhibiting a tightening of budgets (in the developed world) and continued need in the developing nations.

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