Proposal for Exploring Collaborative Research Opportunities in Wound Care using Conventional Medicine and Traditional Chinese Medicine

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Summary

Chronic wounds affect 60 million people worldwide and cause a heavy burden on patients, families, and society. Although various treatments are available in western medicine, chronicity and delayed healing of wounds continue to impair lives. In China, cost-effective traditional Chinese medicine (TCM) has been used for thousands of years for the management of various chronic wounds. However, due to lack of availability and lack of research evidence, TCM treatments are not widely accepted in the United States. As TCM is gaining popularity throughout the world, an increasing number of people are gaining access to TCM therapy in the United States. As a result, there is a growing need to explore the possible benefits of traditional Chinese medicine on wound healing. Research studies comparing TCM and western approaches to wound healing may lead to more efficient and new technologies for wound healing in the future.

The objective of this initial work is to explore the possibilities of combined research studies using both western medicine and TCM in wound care. The empirical work will mainly be comprised of visits to the Center for Wound Healing Research at Daemen College and Dr. Tang’s Lab at Beijing University of Chinese Medicine (BUCM). After full exposure and acculturation to research techniques and personnel in both institutions, the student researcher will draft a research proposal. The proposal will focus on collaborative research to investigate the integration of TCM and western modalities for the treatment of chronic wounds. Following these initial steps, subsequent research proposals will be submitted with hopes of securing external funding from both
Chinese and American agencies.

**Statement of need**

Chronic wounds are wounds that do not heal, as compared to acute wounds, which follow a normal recovery path. All wounds originate in the acute stage of healing and derive from a variety of reasons including trauma, surgery, sickness, or bodily inadequacies, such as venous insufficiency. In general, any trauma that leads to tissue damage can result in a wound. Chronic wounds arise from conditions including diabetes, venous hypertension, alterations in health status, and immune function suppression.¹ Acute wounds become chronic wounds when biological and environmental factors combine to create a wound environment that fails to support a natural and timely healing process.² Many experts consider a wound chronic when it no longer follows the expected course of events or falls within the range of what is considered a normal healing trajectory.³ Interruptions within the typical healing process occur more readily as the age of the patient increases and as the health condition of the patient decreases. Chronic wounds fail to respond to treatments, possess an unhealthy tissue quality, and fail to achieve proper closure, which leaves the wound susceptible to infection.¹

Because of the various ways chronic wounds form, a variety of categories of chronic wounds exist. The main categories of chronic wounds include the following: venous stasis ulcers, diabetic ulcers, pressure ulcers, and any other wound that fails to heal properly.⁴,⁵ Venous ulcers form from venous insufficiency caused by the improper pumping of fluids through vessels within muscle. With this improper propulsion force, fluids within vessels become trapped, and cellular components within the fluids seep into surrounding tissue, which causes damage and/or tissue breakdown.⁶ Other chronic wounds form due to alterations in sensory functions. In individuals with
diabetes, alterations in sensation of the distal extremities can contribute to the formation of diabetic ulcers. Patients who experience interruptions in sensory processing fail to realize an injury has occurred and neglect to carry-out necessary precautions, such as limiting weight-bearing or decreasing shear forces applied to the wound, to allow healing to occur.\(^6\)

A separate primary chronic wound category is comprised of pressure ulcers. Pressure ulcers result from compressive forces or shear forces applied to areas of tissue, which restrict blood flow.\(^7\) When pressure on vessels impedes blood flow, further tissue damage can result. Pressure ulcers are characterized by deep tissue necrosis and loss of volume that are disproportionately greater than the overlying skin defect.\(^7\) Ultimately, pressure ulcers appear small at the skin surface; however, the majority of the wound may exist below the surface at a more critical stage.\(^5\)

Chronic wounds may lead to a number of complications including disability or need for assisted living, home care, depression, loss of digit or limb, infection, or even death. Symptoms and complications associated with chronic, non-healing wounds may destroy an individual’s mobility and quality of life. Approximately 60 million people worldwide are being treated for chronic, non-healing wounds. The public health and economic impact of chronic wound care is staggering, with an estimated annual cost upwards of more than 8 billion dollars (US).\(^8\) In the United States, chronic wounds affect 5.7 million patients. The total direct cost of treating chronic wounds in America, which includes wound diagnostic and surgical procedures, pharmaceuticals, wound closure devices, and hospital and physician charges, amounts to an estimated $20 billion (US) annually.\(^9\) Additional indirect costs of chronic wounds are the result of lost work time and impaired quality of life.\(^10\)

Until recently, chronic wound management in Western medicine has been limited to bandages
and medications, which can lead to very slow and painful recovery processes, increased spread of infections, and longer hospital stays. Other widely-used advanced therapies include bioengineered skin substitutes, electrical stimulation, hyperbaric oxygen therapy, advanced drug delivery systems, materials that repair tissue (platelet-derived and autologous growth factor), and ultrasound. On the other side of the world, TCM has been used in China for thousands of years for the management of various chronic wounds. Chinese herbal therapy is both internally used and externally applied as the mainstream treatment in TCM wound care, and various ancient and modern TCM literature has documented the use of herbal formulae like Wuwei Xiaodu Yin (detoxification drink with five herbs), Huanglian Jiedu Tang (detoxification decocation with huangliangen), Yanghe Tang (decocation for yang harmonization), Tuoli Xiaodu San (power for defensive qi enrichment and toxicant removal), Shengji Yuhong Gao (red ointment for granulation promotion), and Shengdan (pellet made from mercury, nitrate, and alumina) in wound care. With the same philosophical perspective of holism and syndrome differentiation, other TCM treatment modalities like cupping, acupuncture, and moxibustion have been found effective in promoting wound healing as well.

Although TCM is still being used for wound care in almost every Chinese hospital, TCM treatments are not widely accepted in the United States. This is due to lack of high quality wound research studies and limited availability of TCM in the United States. As most states of the United States have legalized the practice of Chinese medicine and acupuncture and more graduates from oriental medicine institutions have been practicing, TCM may eventually contribute more to the general welfare of the American people, which include patients with chronic wounds. Therefore, exploration of the possible benefits of TCM on wound healing is necessary.

Chronic wound healing is a complex process and is often complicated with co-morbidities
including diabetes and obesity. Although various treatments are available in western medicine for those suffering from open wounds, chronicity and delayed healing continue to impair lives and, in some cases, cause death. The United States is an aging society and as disorders like diabetes and obesity increase in prevalence, the importance of improving clinical treatment and outcomes for those with chronic wounds becomes paramount. The associated morbidity, mortality, and treatment costs of chronic wounds increase the need for better outcomes. In order to develop better treatment for chronic wounds, we need to study the possible benefits of TCM treatments and compare conventional medicine and TCM treatments in wound care. However, for the first step, we need to explore the possibility of collaborative research and become more familiar with both western medicine and TCM as they relate to wound research and wound care.

**Feasibility**

Founded in 1956, the Beijing University of Chinese Medicine is one of the earliest established traditional Chinese medical institutions for higher TCM education in China. It is the only TCM institution incorporated into the “National 211 Project” a project of National Key Universities and colleges initiated in 1995 by the Ministry of Education of the People's Republic of China, with the intent of raising the research standards of high-level universities and cultivating strategies for socio-economic development. Presently, the University consists of a School of Preclinical Medicine, Chinese Materia Medica, Acupuncture, Moxibustion & Tuina, Administration, Traditional Chinese Nursing, Distance Education, Continuing Studies, Chinese Clinical Medicine, Humanities & Social Science, an International School, a Department of Chinese Medicine for Taiwan, Hong Kong and Macao, and several large tertiary level hospital in the Chinese capital Beijing. Researchers at the university have conducted a great amount of research studies
both in western medicine and TCM.

Dr. Minke Tang, a research scientist and professor at BUCM, served as a research scholar at the University of Pittsburgh and University of California at Davis while visiting the United States. He is an expert in fundamental research studies of herbal products, especially Salvianolic acid B, which is an herbal extract that may be useful for wound care.

Daemen College, a private liberal arts college with a history of more than 60 years, is known for its physical therapy, physician assistant, and nursing programs in the United States. Researchers at its Center for Wound Healing Research, led by Dr. Laura Edsberg, have carried out various fundamental research studies and clinical trials in wound care. During the past several years, researchers in the center have identified protein S100A9 as a potential biomarker of wound healing\textsuperscript{13} and evaluated treatments for wound care.\textsuperscript{14}

Cooperation between Daemen College and BUCM started in 2005 when Daemen sent Dr. Brogan and Dr. Edsberg to BUCM to teach a course focused on wound care. In an agreement signed in September 2006, by the presidents from both institutions at that time, the two institutions agreed to carry out student and faculty exchange as well as cooperation in wound research. During the past five years, significant progress has been made for strengthening this relationship between two institutions. Daemen accepted its first group of exchange students from BUCM in 2006, and the first group of Daemen students went to BUCM in 2007. Daemen welcomed the first BUCM exchange faculty member Dr. Zhang, a Fulbright scholar in 2009, and more than ten Daemen faculty members have visited BUCM since 2005. However, little progress has been made in collaborative wound research.

This project will further develop and facilitate collaborative research between BUCM and
Daemen College. The proposed research is the first of what is envisioned as a series of projects intended to build a cooperative research algorithm regarding fundamental and advanced research studies along with future clinical trials in wound care which bridge TCM and western medicine, thereby establishing more efficacious treatment for chronic wound care in the United States and China.

The initial task of this overarching project will be carried out by Kehua Zhou, a fifth year Doctor of Physical Therapy student, who graduated with a master’s degree in TCM from BUCM in 2010. The research program will be based on the relationship between BUCM and Daemen College. Main participating personnel will include Dr. Tang (BUCM), Dr. Brogan, and Dr. Edsberg (Daemen College). With the supervision of Dr. Edsberg and support from Dr. Tang and Dr. Brogan, the student researcher will compose a final research proposal for integrated wound research and submit this proposal to associated Chinese and American funding agencies for future funding.

**Proposed work in the coming fall**

**Phase I** (Sept.-Dec., 2011): Communication between both institutions (BUCM and Daemen College) and training at the Center for Wound Healing Research (Daemen College). The student researcher will observe and engage in ongoing biochemical research projects for perspective and experience, and he will communicate with associated personnel in both institutions to further develop strategies for future research projects. The tasks of this training consist of mastering the skills and techniques commonly applied in modern wound research. In addition, the student researcher will also explore possible future directions of research under the supervision of Dr. Edsberg and Dr. Brogan. As a result, a review paper will be written at the end of this phase regarding chronic wounds, proteomics, and current research in the literature relative to TCM and proteomics.
**Phase II** (Dec., 2011 - Jan., 2012): Visit to Dr. Tang’s Lab in BUCM, China, and observe research and techniques utilized in the study of herbal products. Visit to TCM hospitals in Beijing, and exposure to common treatment methods used in chronic wound care in these hospitals. In addition, the student will also explore possible future directions of research under the supervision of Dr. Tang. As a result, a review paper regarding research of herbal products, TCM treatments of chronic wounds, and potential proteomic research areas related to both.

**Phase III** (Feb, 2012): At the end of phase 2, a summary will be submitted to the Daemen College exploring possible collaborative research projects in wound care. After discussion with associated personnel at these two institutions, a collaborative research proposal will be written and presented to Dr. Brogan, Dr. Edsberg, and Dr. Tang for final review. Finally, with agreement of associated personnel from both institutions, the research proposal will be submitted to Chinese and/or US government agencies for potential future funding.

**Phase IV** (Fall, 2012 and thereafter, not included in the initial proposal): develop proposals for external funding which bridge the implicit nature of both TCM and western medicine as they relate to wound care.

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