# AloeMD

*Cellular Matrix Stabilization Through Nutraceutical Biomodifiers*

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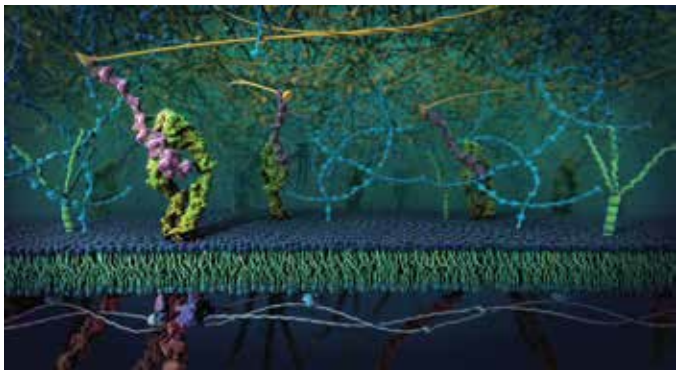

### The Extracellular Matrix (ECM)

In cell biology, the term "extracellular matrix" (ECM) refers to the extracellular part of mammalian tissue that provides structural support to the cells, and performs various other important functions. ECM is the defining feature of connective tissue in animals, and includes the interstitial matrix (present in the intracellular spaces around various mammalian cells) and the basement membrane (sheet-like depositions of ECM on which various epithelial cells rest). It provides support and anchorage for cells, sequesters cellular growth factors, regulates inter-cellular communication, and segregates or compartmentalizes various types of cells that are contained within the matrix.

The interstitial space is composed of a number of biological molecules, including, glycosaminoglycans (GAG) and fibrous proteins that form an interlocking mesh. These act as a compression buffer against the stress placed on the ECM. Glycosaminoglycans consist of repeating disaccharide units. Hyaluronan (HA) lacks any sulfate groups, but the rest of the GAGs contain sulfates at various positions.

Formation of ECM is essential for processes like cell growth, tissue differentiation, wound healing and fibrosis. An understanding of the complex structure and function of the ECM also helps facilitate analysis of the dynamics of tumor invasion and cancer metastasis, which often involves destruction of ECM by matrix metalloproteinases and serine and threonine proteases.

Components of the ECM are produced intracellularly by resident cells, and secreted into the ECM via exocytosis. Once secreted, they aggregate with the existing matrix. As described by Varki et al. (1999), the ECM determines the physical characteristics of tissues and many of the biological properties of cells embedded in it. Major components of the ECM are fibrous proteins that provide tensile strength (e.g., various collagens and elastin), adhesive glycoproteins (e.g., fibronectin, laminin, elastin, and tenascin), and proteoglycans that provide a hydrated gel that resists compressive forces.

Proteoglycans consist of a core protein and one or more covalently attached GAG chains. GAGs are linear polysaccharides, whose building blocks (disaccharides) consist of an amino sugar (either GlcNAc or GalNAc) and uronic acid (GlcA and IdoA). Virtually all mammalian cells produce proteoglycans and either secrete them into the ECM, insert them into the plasma membrane, or store them in secretory granules. The matrix proteoglycans include small interstitial proteoglycans (e.g., decorin, biglycan, and fibromodulin), a protoglycan form of type IX collagen, and one or more members of the aggrecan family of proteoglycans (e.g. aggrecan, brevican, neurocan, and versican.)

Some of these proteoglycans contain only one GAG chain (e.g., decorin), whereas others have more than 100 chains (e.g., aggrecan). The matrix proteoglycans typically contain the GAGs known as chondroitin sulfate (CS) or dermatan sulfate (DS). Exceptions to this generalization exist, since the heparan sulfate (HS) proteoglycans, perlecan and agrin are major species found in basement membranes. A number of different types of proteoglycans are also found within the ECM, including keratin sulfate.

### Disruption of the Matrix

Disruption of the ECM in mammalian tissues has been implicated in a number of disease processes. ECM deterioration has been associated with poor prognosis of many types of connective and hyperproliferative disorders. In particular, destabilization of proper ECM structure and function in human tissues, such as breast and prostate tissues, has been shown to aggravate the disease process in those organs. This disruption manifests itself in a number of indications, including over expression of tRAS, inflammation, infection, loss of tissue integrity and biochemical imbalances in the cells contained within the matrix, and can lead to increases in mammographic density, microcalcification, degeneration of healthy tissue, and a number of neoplastic and other disease processes in situ.

Certainly there is a need for compositions that improve the health of ECM-rich mammalian tissues, limit ECM deterioration and dysfunction, increase stabilization of the ECM and its resident cellular cooperative, and reduce, eliminate, or prevent harmful cellular processes such as aberrant tRAS angiogenesis, inflammation, microcalcification, and the development of neoplastic disease.

### Disease of the Breast

Disease of the breast is currently rising in the American population at an alarming rate. Fibrocystic changes, fibroadenomas, and breast cancer have even been termed by some as reaching "epidemic" proportion. Statistics show that breast cancer is the second leading cause of death in women ages 20-59. In the United States, a new breast cancer is diagnosed every 3 minutes, with approximately 63,000 new cases of carcinoma in situ (CIS) being reported annually. The incidence of ductal CIS (DCIS) rose from 1.87 per 100,000 in 1973-1975 to approximately 32.5 per 100,000 in 2004. Alarmingly, over 40,000 women in the US die from breast cancer annually. Unfortunately, for those with advanced forms of the disease, chemotherapy has not significantly affected long-term survival rates.

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## Cellular Matrix Stabilization Through Nutraceutical Biomodifiers

Prevention of breast cancer, or any cancer for that matter, has been an elusive goal, especially when employing the current medical paradigm. Since the Nixon administration declared "war on cancer" in the 1970s, a great deal of research and money has been devoted to achieving this end. Unfortunately, the battle remains unwon, despite valiant efforts across both research and treatment fronts. In spite of billions of dollars allocated for this "war," relatively little progress has been made, particularly in its prevention or increasing the long-term survivability of people with advanced metastatic disease. Although many (and oftentimes, expensive) chemotherapeutic agents are at a physician's disposal, the ultimate solution for winning the battle with cancer still eludes even the brightest contemporary minds. Currently this is only a 2.3 % increase in survival rates using chemotherapy.

The failure to win the war, however, is not from lack of resource allocation, but from a faulty plan of attack based solely on the prevailing paradigm of intervention at the cellular level. Medicine's current view of early carcinogenesis focuses on the relationship of the cell as the driving force behind the neoplastic process. This has been termed as the "somatic mutation theory" or SMT, which argues that an accumulation of mutations and other heritable changes in the susceptible cell can result in cancer. The SMT paradigm, however, is not without its critics. Problems with its basic tenets have been noted in a number of scientific publications by Kolata, Sonnenschein, Soto, and other well-known artisans in the field.

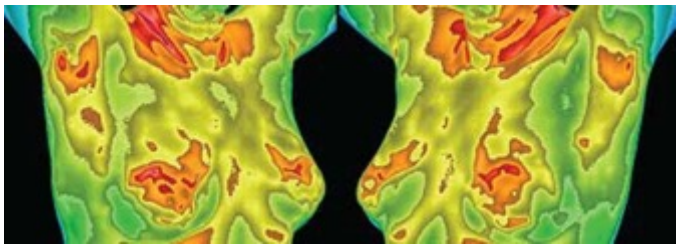
We have noticed various observations, however, that question the validity of the SMT paradigm. These observations include: 1) mice fitted with subcutaneous filters that have small holes give rise to tumor formation while mice fitted with the same filter material but having only larger holes remained tumor-free; 2) transplantation of normal rat mammary cells into adjacent stroma (which was cleared of local epithelia cells but previously exposed to a chemical carcinogen) results in a much higher tumor rate as compared to controls; and 3) transplantation of normal cells into untreated, but "inappropriate," stromal environment induced carcinoma formation. Yet, these now abnormal cells returned to a normal state upon transplantation back into their original "appropriate" stromal environment, concluding that the ECM plays a vital role in cancer formation and signaling.

## Thermography and Human Breast Tissue

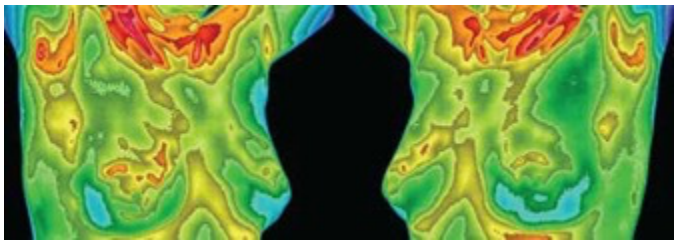
Thermograms consist of digital infrared imaging that produces high resolution pictures of temperature variations found in tissue. Increases in temperatures denoted by the color red indicate potential issues such as inflammation-induced excessive/atypical blood flow, tissue damage,increased cell metabolism, and hormone imbalances. Each of these biologic processes acts to increase the entropy residing within the ECM. A stable physiologic microenvironment has a higher ordered state that translates into lower entropy.

Thermograms, therefore, provide a functional assessment of the human tissues, such as breast tissue, including a quantitative measurement of those events that disrupt the ECM.

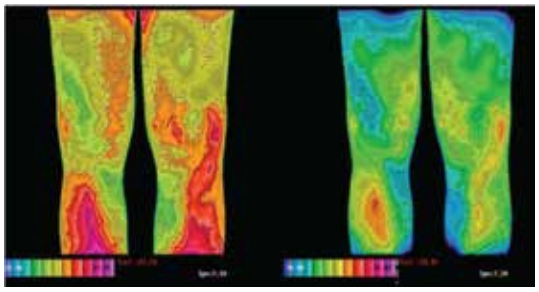
Pro-angiogenic and pro-inflammatory pathways, studied by other in vivo models, can be measured in the form of pixels. The effectiveness of an exemplary transdermal orthomolecular formulation in accordance with one aspect of the present invention to stabilize the ECM of human breast tissue was measured using breast thermography.



Pre-AloeMD Cream Thermography



Post-AloeMD Cream Thermography



Before After

Human clinical testing with AloeMD Cream resulted in significant relief of joint pain and inflammation. Additionally, clinical evaluation of AloeMD Cream using thermography along with standard radiographic modalities revealed stabilization of (ECM) by reduction of aberrant blood flow.

## AloeMD Therapeutic Cream

An orthomolecular transdermal cream with enhanced tissue absorption designed to stabilize the extracellular matrix (ECM) of the breasts and other tissues.

An intact ECM supports cell, tissue, organ, and organ system integrity by providing for proper physiologic functioning of each biologic entity. Chronic alteration of this microenvironment resulting in a prolonged state of dysfunction will lead to end-stage structural alterations that are termed "pathological." Stabilization of the ECM represents a defense against the onset and progression of chronic disease. AloeMD Cream may work to decrease prolonged ECM disruption represented by various chronic disease states.

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### Scientific Validation

In-Vivo Tested, Clinical Efficacy, Clinically Proven

Fig. 1 shows the effect of pre-treatment on oxazolone-induced murine ear edema, and graphs a second, formalized in vivo study outcomes illustrating the reduction of oxazolone-induced ear edema using acetone control, topical betamethasone, AloeMD Cream and oral celecoxib.

Fig.1

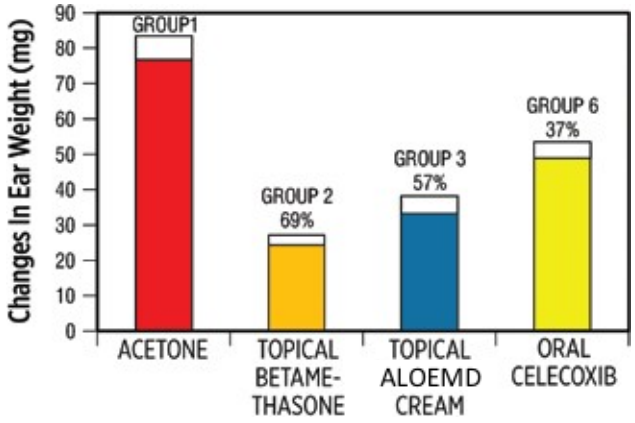
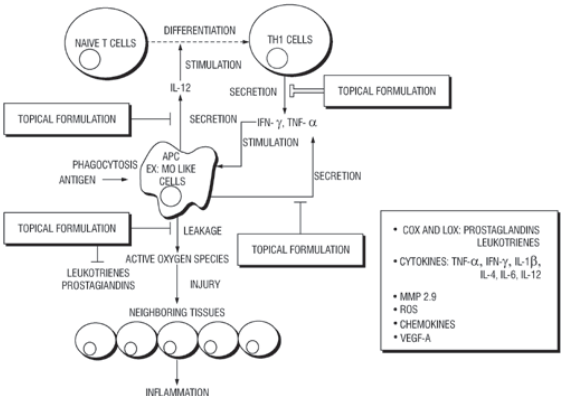


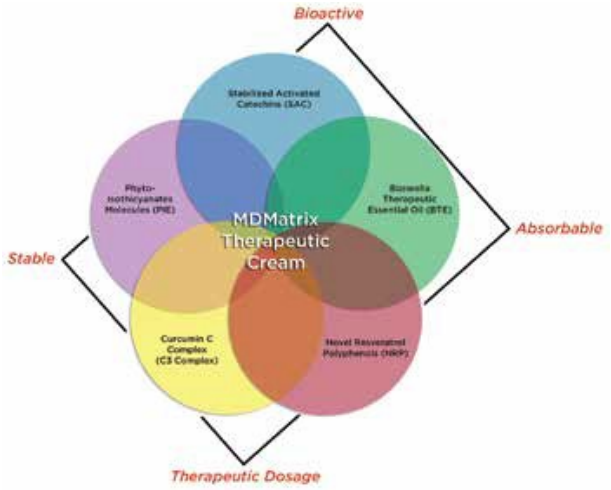

Fig. 2 shows the oxazolone-induced murine ear edema model is based on cells that exist within the stromal ECM.

Fig. 2




AloeMD Therapeutic Cream may help improve chronic inflammation and other disease states by providing a new and useful composition which could improve mammalian cellular function, promote healthy tissue development, reduce inflammation, and/or stabilize one or more components of mammalian ECM.

AloeMD Therapeutic Cream advantageously provides a multi- component nutraceutical composition and formulation which may facilitate stabilization of the ECM and may provide a deterrent to chronic diseases, and in particular diseases of inflammatory origin. AloeMD Therapeutic Cream has demonstrated that successful stabilization of the ECM can decrease the morbidity of chronic processes by reducing pain and preserving healthy organ function.




### Dr. Joseph McWhereter, MD, FACOG, FACS

**Chief Medical Officer- HW&B Enterprises, LLC**

Joseph F. McWherter, MD, is board certified in Obstetrics and Gynecology. Dr. McWherter received his undergraduate degrees in physics and mathematics in 1973 from the University of Texas at Austin. Upon attending the University of Texas Health Science Center at Dallas, he was awarded a medical degree in 1977 and completed his residency in Obstetrics and Gynecology in 1981. Dr. McWherter's professional memberships include being a Fellow of the American College of Obstetrics and Gynecology, a Fellow of the American College of Surgeons, a Member of the American Medical Association, a Member of the Tarrant County Medical Society, a Member of the Texas Medical Association, a Member of the Association of American Physicians and Surgeons, a Member of the Society of Laparoendoscopic Surgeons, a Member of the North American Menopause Society, a Member of the Institute of Functional Medicine, a Member of the American Society for Reproductive Medicine (previously the American Fertility Society), a Member of the Endocrine Society, and a Member of the American Institute of Ultrasound Medicine. Dr. McWherter was awarded the prestigious Alan P. Mintz, M.D. Award for Excellence in Age Management Medicine. He also has served as chairman of the peer-review planning committee and speaker for the Integrative Medicine for Anti-Aging Conference and Exposition.

Dr. McWherter is the Medical Director of the FEM Centre and Energy Health Centre offices in Colleyville and Fort Worth, Texas. He has helped thousands of women find optimal health and wellness through hormonal balancing. As an innovator in the fields of women's health and anti-aging, Dr. McWherter believes that a thorough approach to health care includes preventative measures.

*"Traditional medicine views the body as a combination of individual components that function independently of one another. Instead of treating the gastrointestinal, cardiovascular, immune, neurological, and hormonal systems as separate entities, I view them as one unified family. Everything in your body is interrelated. If you look at each function as an isolated system, you end up treating only the symptoms of a disease, not the root problem."*

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