# WHITE PAPER

# THE AGE OF









# It's the Age Old Story:

As cliche' as it may sound, the world's population is aging. Increasing longevity and declining fertility have combined to change the population age structure worldwide from younger to older—an historic demographic transition which is still in progress. In the United States, the population over age 65 will almost triple by 2070 and the population over 85 will increase fivefold (see table; US Census Bureau). In

addition, the average age at retirement in the U.S. has decreased from 74 in 1920 to 62 in 2000. Americans now live long and often productive post-retirement lives. In tandem with factors related to aging, we find ourselves in a more complex world filled with various stress factors that serve as catalysts for various forms of bodily disease. Emotional stress, environmental and nutritional poison, poor quantity and quality of exercise, physical and emotional trauma, and an overall weakening constitution are some of the key factors that negatively affect our health and well-being.

PROJECTED INCREASES IN OLDER U.S. POPULATION				
	2000 (millions)	2025 (millions)	2050 (millions)	2070 (millions)
Total Population	275	338	404	464
Ages 65 and older	35	63	82	98
Ages 85 and older	4	7	19	23

Today, chronic diseases—such as cardiovascular disease (primarily heart disease and stroke), cancer, diabetes—are among the most prevalent of all health problems. Seven of every ten Americans who die each year (more than 1.7 million people) die of a chronic disease. The prolonged course of illness and disability from such chronic diseases as diabetes and arthritis results in extended pain, suffering and decreased quality of life for millions of Americans. Chronic, disabling conditions cause major limitations in activity for more than one of every ten Americans. (Source: CDC; 2007)

### Joint Ownership of a Pervasive & Painful Problem:

One of the most predominant problems shared by the world-wide aging population are physiological conditions affecting "joint health." A human being has 206 bones and over 230 moveable and semi-



moveable joints in the body. As we age, the wear and tear on our bodies naturally accelerates. A breakdown of the skeletal system in the form of various arthritic conditions is common, specifically at points where the bones articulate, resulting in pain, inflammation, stiffness and a compromised ability to perform our daily tasks and responsibilities.

It's interesting to note that "arthritis" is a term used to describe more than 100 different conditions affecting joints, as well as other parts of the body. Arthritis has plagued mankind for millennia. Historians have found references to forms of arthritis in Greek and Roman literature, and some even suspect cavemen suffered from it. Arthritis is one of the most prevalent chronic health problems and the leading cause of disability in the US. According to the Arthritis Foundation® we are "a nation in pain." This is further supported by the following series of statistics:

- An estimated 46 million adults in the United States reported being told by a doctor that they have some form of arthritis, rheumatoid arthritis, gout, lupus or fibromyalgia.
- Arthritis affects more than 34 million Caucasians, more than 4.5 million African Americans and nearly 2.6 million Hispanics.
- One in five (21%) adults in the United States report having doctor-diagnosed arthritis.
- By 2030, an estimated 67 million of Americans aged 18 years or older will have doctor-diagnosed arthritis.

- Arthritis costs the U.S. economy \$128 billion annually.
- Nearly 80 percent of adults either have or know someone with arthritis.
- In 2002, 51% of adults 75 years and over reported an arthritis diagnosis.
- Arthritis prevalence increases with age, among adults over age 65, the prevalence of arthritis is 48 percent.
- The prevalence of arthritis is higher among women (25.9%) than men (16.8%).
- If prevalence rates remain stable, the number of affected persons ages 65 years and older will nearly double to 41.1 million by 2030.
- Arthritis annually results in:
  - 39 million physician visits
  - 744,000 hospitalizations
  - 3 million visits to outpatient departments
  - 2.2 million visits to emergency room departments
- Arthritis is the third leading cause of work limitation in the United States.
- Nearly 300,000 children under the age of 17 are affected by juvenile arthritis.



### Boning Up on the Cause of the Problem:

Given the prevalence of the problem, all of us at one time in our lives are candidates for joint difficulties. It's important to take a look at some of the more common causal factors.

#### Aae:

Age is a key factor. Cartilage becomes more brittle with age and has less of a capacity to repair itself.

#### Weight.

Excess body weight is another cause because joint damage is partly dependent on the load the joint has to support. This is especially true of the hips and knees that can be worn quickly in those who are heavier.

#### Diet.

Improper nutrition can stimulate inflammation and exacerbate joint function. A plethora of foods devoid of meaningful value are available on today's market that serve as irritants to various part of the body and cause disease.

### Genetics:

Family genetics or physiological propensities are passed down from generation to generation. These genetic variations can contribute to a condition such as arthritis and other joint problems.

#### Previous Injury:

Joint damage can cause irregularities in the normal smooth joint surface. Sports injuries as example, are a common cause of arthritis.

### Illness or Infection:

People who experience a joint infection (septic joint), multiple episodes of gout, or other medical conditions, can develop arthritis of the joint.





Many types of arthritis are "inflammatory" disorders. For the record, arthritis literally means an inflammation (itis) of the joints (arthr). When joint inflammation occurs, the increased number of cells and inflammatory substances within the joint cause irritation, wearing away cartilage (the cushions at the ends of the bones), and causing swelling of the joint lining. Furthermore, chemicals from the body are released into the blood or affected tissues which increase the blood flow to the area of injury or infection and often result in redness and warmth. Some of the chemicals cause a leak of fluid into the tissues, resulting in swelling. This process may stimulate nerves and cause pain. Increased blood flow and release of these chemicals attract white blood cells to the sites of inflammation. The increased number of cells and inflammatory substances within the joint can cause irritation, wearing down of cartilage and swelling of the joint lining (synovium).

Symptoms indicative of the inflammatory process includes:

- · red, swollen joints which are warm to the touch
- joint pain and stiffness
- loss of joint function

# The Inflammation Syndrome:

One condition that explains our stiff fingers, aching muscles and arthritic joints, and that lies at the root of our troublesome allergies and asthma, as well as the underlying cause of heart disease, Alzheimer's disease, and some types of cancer is inflammation.

Most of us understand inflammation as something that causes redness, tenderness, stiffness and pain. It is the core of inflammatory "-itis" diseases, and it is intertwined in every disease, including obesity, diabetes and multiple sclerosis. Inflammation is why professional athletes and weekend warriors often develop muscle aches. It is why some people's gums bleed whenever they brush their teeth. And it's why some people develop stomach ulcers.

Despite their different symptoms, all of these health problems are united by the same thread: they all have runaway inflammation in common. Many people suffer from more than one inflammatory disorder. Such a constellation of related diseases, such as the combination of heart disease, arthritis, and periodontitis, can be best described as the "inflammation syndrome". Millions of North Americans suffer from inflammatory disorders, some of which have only recently been recognized as inflammatory in nature. The following estimates the number of North Americans with some form of inflammatory disease:

INFLAMMATORY DISEASE/NORTH AMERICA			
	Millions		
Allergic and Non-Allergic Rhinitis	39		
Asthma	17		
Cardiovascular Disease	60		
Arthritis (all types)	44		
Osteoarthritis	21		
Rheumatoid Arthritis	2		

Source: "Inflammation Syndrome" (Jack Challem; © 2003)



Everyone experiences inflammation at one time or another, and we actually need it to survive. But chronic inflammation is a sign that something has gone seriously awry with our health. Instead of protecting and healing, chronic inflammation breaks down the body and makes it older and more frail. In today's world, most people treat inflammation with one or more over-the-counter and prescription drugs. At best, these drugs temporarily mask the symptoms of inflammation, while not treating its underlying causes. Worse, the side effects of these drugs can often be extraordinarily dangerous, causing weight gain, severe stomach pain, bone deformities and heart failure. To understand a major cause of the modern epidemic of inflammatory diseases, we have to look at diet, which has deteriorated over the past two or three generations, and how food has influenced the onset of inflammation.

Until relatively recently, people ate a relative balance of pro- and anti-inflammatory nutrients. Today, because of extensive food processing, our diet has become seriously unbalanced. The typical Western diet now contains at least 30 times more pro-inflammatory nutrients than just a century ago. As a result, people have become nutritionally and biochemically primed for powerful, out-of-control inflammatory reactions. An injury, infection and sometimes nothing more than age-related wear and tear create the spark that, in a manner of speaking, sets your body on fire.

### Some Forms of Treatment have Skeletons in the Closet:

There are standard pharmaceutical and over-the counter drug options available whose primary goal is the relief of pain and discomfort without ever getting to the "root" cause of the problem. Drug alternatives such as NSAIDS (non-steroidal anti-inflammatory drugs) and Cox-2 inhibitors may temporarily relieve symptoms associated with arthritis, but side effects such as gastrointestinal and cardiovascular problems are common.

Many OTC pain relievers are also available on today's market, but the risks associated with their long term use is often much greater than their rewards. According to AC Nilesen, dollar sales in 2006 of topical and internal analgesics in FDM retail outlets are estimated to total \$312 million and \$2.4 billion respectively. These numbers do not include analgesic sales in the world's largest retailer, Wal-Mart.

As America ages and millions find themselves suffering with various arthritic conditions, a growing number of pain sufferers have decided to go the "natural" route, and make efforts to better understand their health issues from a "wholistic" perspective. This growing population has one thing in common: to gain a deeper understanding of the underlying root cause of their health problems so that real physiological balance can ensue. It certainly makes sense to hold this point of view when working towards optimum health and well-being. If we allow the normal instinctive bodily healing processes to unfold, while at the same alleviating the pain and discomfort of various forms of dis-ease, it's a win-win for the health and well-being of the physical body as well as our quality of life.



This positive alternative medicine trend can be seen in the growth of nutraceutical sales world-wide. According to Nutrition Business Journal, product sales of the global nutritional industry are now estimated at \$228 billion. NBJ projects U.S. nutrition industry sales growth at \$85 billion in 2006, +10% in comparison to the prior year. This was its highest annual growth since 1998. The nutritional supplement segment topped \$24.5 billion with an overall 5% rate of growth from year to year.

In record numbers, consumers en masse are seeking natural supplementation to repair and revitalize their bodies and deal with problems related to their joints. This trend can be confirmed clearly with the rising popularity of Glucosamine. Used clinically in Europe since the 1960's, glucosamine regularly combined with chondroitin sulfate became very popular in the United States in the mid-1990's with the publication of popular best-sellers such as "The Arthritis Cure" by Jason Theodosakis. It is now one of the most popular dietary supplement in the United States. In the last 52 weeks, in the FDM channel exclusively (without Wal-Mart), sales of glucosamine were \$310 million dollars.



### Getting to the Root of the Problem with Celadrin®.....Naturally:

It isn't often that a natural product comes along within the nutritional supplement medicinal category that's totally unique and experiential to the consumer. It's even more rare that the product raises the bar on quality and efficacy to a new and unprecedented level. Celadrin is such a product, providing an all-natural and effective solution to a wide-scale problem now at epidemic heights.

Celadrin is comprised of innovative, targeted and proprietary cetylated fatty acid esters and other active synergists. It's a proprietary natural compound that's scientifically designed to be absorbed rapidly and provide immediate and continuous results. Celadrin is available in either oral or topical dosage forms, and has been shown to be safe & efficacious as evidenced by medical journal published gold standard, double-blind, placebo-controlled clinical and scientific studies and has no side-effects. Celadrin® is FDA compliant and non-prescriptive.

We've discussed the importance of getting to the root cause of serious and significant health problems. Relative to the numerous afflictions that fall within the arthritis disease grouping, extinguishing the inflammatory fire is essential if real healing is to take place. Celadrin acts very effectively to smother this fire, but in order to better understand how it acts to accomplish this goal, let's bring our attention to the body's cellular level.

The body is made up of many cells separated into various types and functions. The cell membrane is the organized structure separating and protecting components within the cell from neighboring cells and the outside world. Some of the major components of the cell membrane are structural lipids or fats. These lipids play an essential role in the regulation of nutrients, minerals, electrolytes and other compounds across the cell membrane. This regulatory process is critical to the adequate function and health of the individual cell and the body at large.

Loss of cell membrane integrity from internal and external stressors begins a number of rapid destructive processes – including uncontrolled or imbalanced inflammation. Inflammation can occur with age, dietary conditions, actions related to free radicals, stress or other conditions which stimulate or "stiffen" and compromise the integrity of the cell's membrane. This often leads to one or more forms of arthritis (bursitis and tendonitis included); periodontal disease, wrinkles, cardiovascular disease (CVD), rapid aging and other serious maladies.



Celadrin® not only halts the cascade of inflammation but rapidly begins to restore the body's physiological balance and its instinctive healing processes. By providing continuous lubrication, Celadrin allows the cell membrane to repel destructive inflammatory chemicals and to become more flexible and stronger. In the process, the cascade of inflammation is stopped, the fluids that cushion bones are enhanced, joint flexibility and mobility are restored, and pain is eliminated. If used for the sake of appearance, the skin is naturally nourished and worrisome wrinkles are reversed in the process.

Celadrin's unique healing action enhances the lipid structure of the cell membrane turning it into a "super membrane" enabling the cells and body to rapidly repair and regenerate. Consuming or applying Celadrin® enables the cell membrane to protect the cell and repel destructive cellular stressors. The result is a more efficient, fluid, elastic, permeable and youthful cell membrane. This unique enhancement of cellular physiology leads to a multitude of restorative, healing and age reversing benefits.





# Celadrin®.....A Special Study in Efficacy and Quality:



In clinical studies using oral and topical applications of Celadrin, patients with chronic knee problems and Osteoarthritis saw significant improvement in knee movement, the ability to climb and descend stairs, rise from chairs, walking, balance, strength and

endurance. More significant was that in one of the clinical studies, patients who were already consuming arthritis medications (Aspirin, Ibuprofen or Celecoxib) still demonstrated significant overall improvement with Celadrin®. Product safety confirmation through Acute Toxicity testing and Ames test screening have also been conducted as part of the scientific process. What follows is a synopsis of some of the clinical studies performed

### **Publications:**

- May 2005: A Cetylated Fatty Acid Topical Cream Reduces Pain and Improves Functional Performance in Patients with Arthritis
  Published in the Journal of Strength & Conditioning.
- Feb 2005: Effects of Treatment With a Cetylated Fatty Acid Topical Cream on Static Postural Stability and Plantar Pressure Distribution in Patients With Knee Osteoarthritis Published in the Journal of Strength & Conditioning.
- Aug 5, 2004: The effects of a cetylated fatty acid topical cream on functional mobility and quality of life of patients with osteoarthritis - Published in the Journal of Rheumatology.
- Apr 1, 2003: Digestion and metabolism of cetylated fatty acids in rats.
- Oct 31, 2002: Distribution of Cetylated Fatty Acids in Rats after Oral or Topical Administration.
- Oct 1, 2002: Digestion and Metabolism of Cetylated Fatty Acids in Rats.
- Sep 17, 2002: A Preliminary Study for the use of Celadrin for the Treatment of Psoriasis.
- Feb 14, 2002: Cetylated Fatty Acids Improve Knee Function in Patients with Osteoarthritis Published in the Journal of Rheumatology.
- Aug 29, 2001: Evaluation of a Topical Cream containing Cetylated Fatty Acids.
- 2001: The Effect of a Cetylated Fatty Acid (CFA) for Improving Quality of Life in Canines.
- 2001: A fatty acid ester (CMC) improves quality of life outcomes in osteoarthritis (OA) patients.

### **Scientific Presentations**

- 2007: The effects of cetylated fatty acid cream on pain, range of motion and quality of life of patients with osteoarthritis.
  Kraemer WJ, Ratamess NA, Anderson JA, Tiberio DP, Joyce ME, Messinger BN, French DN, Sharman MJ, Rubin MR, Gomez AL, Volek JS, Hesslink R Jr.
- 2003: The effects of a cetylated fatty acid cream on functional mobility and performance in patients with osteoarthritis.
  Ratamess NA, Kraemer WJ, Anderson JA, Tiberio DP, Joyce ME, Messinger BN, French DN, Sharman MJ, Rubin MR, Gomez AL, Volek JS, Hesslink R Jr.
- 2003: Absorption and metabolism of a cetylated fatty acid. Islam A, Gallaher C.M., and Gallaher D.D.
- 2002: Digestion and metabolism of cetylated fatty acids in rats. Gallaher D.D., Gallaher C.M., Hesslink R. Jr.
- 2002: The effects of a cetylated fatty acid complex on canine osteoarthritis. Hesslink R.L., and Sprouse S.
- 2001: A fatty acid ester (CMC) improves quality of life outcomes in osteoarthritis (OA) patients. Barathur R.R., Bookout J.B., Sreevatsan S, Freedland E.S. and Hesslink Jr., R.L.

### **Technical Reports:**

- 2002: Bacterial reverse mutation Ames test screening MDS Pharma, Les Oncins, France.
- 2002: Evaluation of topical cetylated fatty acid application to psoriasis patients Dermatologist Medical Group of North County, Inc.
- 2001: The acute toxicology of oral cetylated fatty acid gavage CD-1 mouse model Perry Scientific, Inc.,
- 2000: Evaluation of a topical cream containing cetylated fatty acids using hairless mouse model Perry Scientific, Inc., Study No. 00-1076.

### \* Clinical Study abstracts available upon request

# Strong Growth in Celadrin® Brand Awareness:



There are few companies in the natural products industry willing to educate the consumer via the media on a national basis. These companies understand the value of wide scale messaging as a means of generating wide-scale awareness for their brands. PNI has been willing to step up to the plate and dedicate the necessary resources in support of Celadrin. Thus far in 2007, Celadrin's National Consumer Education and Brand campaign has generated consistent media coverage within targeted geographic and demographic markets.





The high level of media interest and coverage is a result of harnessing a diverse mix of experts and topics that all have one thing in common, the promotion of Celadrin as an effective natural remedy for the woes related to arthritis and other inflammatory conditions.



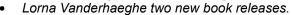
2007 activity continues and planning is currently underway for 2008 which promises to have the most potential yet:

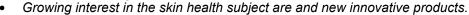


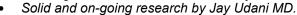
 Growing national interest in the Celadrin Tigerettes, the Huntsman World Games this fall and 2008, WNBA media tour and charity fund raising for the tickets for seniors program.

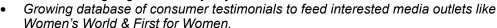


- 2007-2008 NBA season, Atlanta Hawks media touring with NBA All-Star Dennis Scott.
- Dr. Lamb's multitude of problem solution topics and the possible endorsement of the National Strength and Conditioning Association <u>www.NSCA-Lift.org</u>.









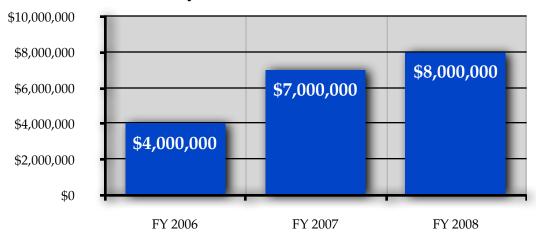




The National branding program generates hundreds of millions of consumer impressions in support of Celadrin. Total projected placements in some of the most widely known TV, radio and print ad vehicles in the US are estimated to generate wide-scale awareness for the Celadrin brand reach millions of dollars in equivalent consumer ad support. National consumer media support during the period of 2006-08 is projected at \$5, \$7 and \$8 million dollars respectively.



## Projected Media Value-Celadrin® 2006-08









The Dallas Morning News





This White Paper has been written to bring to light to a very important breakthrough in the field of nutraceutical science. The various maladies associated with arthritis are more pervasive and critical relative to the aging of America. When we have pain, our first and foremost response is to make it stop. This knee-jerk reaction on the part of millions results in the purchase of any number of unnatural pain relievers on the shelf. For the most part, those who are suffering are not aware of the destructive side-effects that result from the use of pharmaceutical and over-the-counter drugs.

Celadrin represents an all-natural, breakthrough treatment option that's come along at an important point within a growing "pain cycle" in the US and world-wide. It offers an alternative that not only gets to the root cause of arthritic pain and other related conditions, but also provides a natural means of elevating the overall health profile of each and every person who uses it.

Celadrin is also a product that works extremely well with other widely known effective nutraceuticals such as glucosamine. As a powerful "one-two-punch" it empowers glucosamine to perform faster and more efficiently to build joint cartilage and relieve pain. Whether in combination with a synergistic nutraceutical partner such a glucosamine, or used alone, Celadrin is a true healing phenomenon that gets to the root of the problem, and in a real way provides "relief" at a deep and meaningful level. The "Age of Celadrin" has arrived!





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