Concepts of Dietary Peptides: Collagen Hydrolysates

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Health care consumers are increasingly becoming disillusioned by the inability of mainstream medicine to solve their health and dietary problems in a safe, cost-effective, and compassionate way. Their solution is to turn to alternative (complementary) methods of treatment and prevention. As Eisenburg et al[1] points out, not only are they unlikely to tell their physicians about their use of unprescribed therapies, they are healthier as a group than their counterparts.

It is the intent of this paper to present some of the literature regarding the various benefits of collagen hydrolysates that are significant to health care consumers.

What is a hydrolysate of collagen?

A collagen hydrolysate is derived from collagen by a chemical process called hydrolysis. Hydrolysis is the process of splitting a bond and the addition of water. Collagen, the principal structural protein, is the main component of connective tissue. It is indigenous to human and animal bodies. Although over 14 types of collagen[2] have been identified, Type I collagen is the dominant constituent occupying over 90% of the tissue. Collagen fibers are the major constituents in the extracellular matrix of skin, bone, tendon, ligaments and cartilage.[3]

Collagen (hydrolysate) consists of a unique amino acid sequence of a family of proteins or peptides. A typical amino acid composition[4] contains 19 of the essential and non-essential amino acids: essential are threonine, valine, isoleucine, leucine, phenylalanine, methionine, histidine, and lysine, non-essential are glycine, alanine, serine, proline, hydroxyproline, tyrosine, cystine, aspartic acid, glutamic acid, arginine and hydroxylysine. The spectrum and sequence of amino acids of collagen differs greatly from that of other proteins by its high content of glycine and proline and low content of histidine and cystine. Collagen peptides also contain two amino acids not found in other proteins, hydroxyproline and hydroxylysine.

Collagen hydrolysates have been listed as GRAS (generally recognized as safe) by the Food & Drug Administration. A plethora of scientific studies, such as acute toxicity, dermal, sensitization and phototoxicity studies, have shown collagen hydrolysates to be very safe in their present practice of use.

Commercially, collagen and its hydrolysates (peptides) can be derived from animal and human sources, although most medical uses involve bovine derived collagen.

Healthcare uses of collagen and its hydrolysates

Collagen is one of the oldest proteins, phylogenetically, appearing in the oldest invertebrate species. [5] The physical and chemical properties of collagen as a biomaterial make it very useful for a wide variety of applications such as in medical

devices and drugs, industrial, cosmetic and nutritional uses. This paper will discuss the medical and nutritional aspects only.

Medical

From a clinical point of view there is much interest in collagen, because many different diseases are related to disorder in collagen. For example, a better understanding of the spatial structure will give more insight in collagen related disorder diseases. These can be congenital like Ehler-Danlos syndrome, or the consequence of a deficiency like scurvy. In the last 10 years, many collagen-based medical devices have been successfully commericalized[6]. Examples are: wound dressings[7,8,9,10,11], artificial skin, drug delivery agents[12,13], corneal shields[14,15,16], bone repair[17], arterial puncture repair[18], and hemostasis.[19,20,21]

There are many reasons why collagen has become the biomaterial of choice:

- Excellent safety profile
- Natural to the body

- Biocompatible and biodegradable
- Collagen is becoming well-known because of the success of commercial products, i.e. wound care dressings and fillers
- Collagen can be produced in many forms such as powders, films, gels, particulate sprays and sponges

In a number of reports on wound care, collagen has been shown to be beneficial by 1) controlling the evaporation of fluid, keeping the wound pliable and flexible, 2) promoting the development of granulation tissue, 3) diminishing pain, and 4) providing mechanical protection against physical and bacterial insult.[22,23,24] Other clinical reports have indicated that collagen powders exhibit excellent adhesion to the wound, hemostatic properties, tissue fluid (exudate) binding and adequate stimulation of cell reactivity with the formation of a highly vascularized granulation bed.[25]

Films made from *hydrolyzed collagen* (i.e. collagen hydrolysates, peptides) have been used to prevent postoperative adhesions.[26] Operation often induces the fibrous tissue adhesions found frequently in operations of the abdominal cavity and often in tendons and nerves. Undesired tissue damage results in most surgical procedures such as cutting, desiccation, ischemic and manipulative abrasions.

Reports indicate that *hydrolyzed collagen* was tested as a tissue adhesive for suture replacement.[27] *Hydrolyzed collagen* was tested because of its chemical resemblance to connective tissue and its adhesive properties. An ideal tissue adhesive is biodegradable, nontoxic, and readily absorbed so that it does not impose a hindrance to the healing process. *Hydrolyzed collagen* was found to be a useful biomaterial for this application.

Nutritional

It was not too long ago that the value of a food was judged primarily on the basis of the energy it provided. However, scientists have since observed that certain nitrogen containing compounds in our diets were also vital for the normal functioning of our cells.

For example, scientific observations[28-34] revealed that these nitrogen compounds, subsequently called proteins, improved the performance and growth of many animals when their diets contained mostly animal proteins, and growth and performance declined when their diets included mostly vegetable proteins such as corn, wheat and soy. These studies examined amino acids, the building blocks of the bones, muscles and virtually all of the body's soft tissues. All proteins contain some of the amino acids. Only collagen protein is differentiated by containing all 19 amino acids, 8 essential and 11 non-essential (see earlier comments). Essential amino acids are defined as being those we must consume in our diets for good health because they cannot be manufactured by our bodies. Non-essential amino acids are defined as the body being able to synthesize or manufacture them from other dietary sources. It should be understood that non-essential does not mean that the body does not need it, but rather that the body can manufacture it from other sources.

Collagen hydrolysates are "cutting edge nutrients"[35] as defined in an article by M. Walker, MD because it contains amino acids such as arginine, glutamine, and glycine. These amino acids act as agonists to produce a hormone called hGH (human growth hormone). According to Dr. Walker, hGH affects every cell and system, rejuvenating the skin and bones and resulting in some kind of body change that is positive. Natural hGH is made in the pituitary gland. When the body is remiss in developing its own hGH, symptomatic bulging, wrinkling and sagging are noted. Taken from the medical literature, many benefits are seen to occur when hGH is given. Some participants in studies experienced an 8.8 % increase in muscle mass, they showed a 14.4 percent loss of fat, had higher energy, increase in exercise performance and faster wound healing occurred.

When ingested, the proteins' chain of amino acids is broken up in the digestive tract by enzymes and acids, and the individual amino acids are absorbed through the wall of the small intestine and into the bloodstream in the liver. From there they travel to the sites where they are needed most for growth or repair of tissues.

A variety of studies have been completed showing the effects of collagens' amino acids. Deschepper K[36], et al, added protein and amino acids to animal feed resulting in lower carcass fat content, whereas low protein diets resulted in higher carcass fat content. In these studies, the animals' carcass fat and abdominal fat increased as the protein content of the diet decreased. In a study by Yagi[37], the effect of orally administered glutamine on the small bowel encouraged the regeneration of tissue. The level of performance increase in wrestlers was statistically significant in a study by Mourier[38]. It was shown that the combination of moderate energy restriction and amino acids induced significant loss of abdominal visceral adipose tissue (in common terms, abdominal fat). The body synthesizes L-carnitine from the amino acid lysine found in collagen. L-carnitine is known to efficiently convert body fat into readily available fuel, and elevates certain enzymes to "burn" sugars and starches[39].

For many years, the cosmetic industry has been topically applying collagen to the skin as a moisturizer. In a study by Dawson, et al[40], the dietary requirements in rats were altered by adding nitrogen, via the supplementation of amino acids to their daily intake of food. It was observed that an increase in the collagen content was accomplished, resulting in a healthier skin and a less wrinkled look.

In another study involving skin incisional wounds in rats[41], it was concluded that arginine, a major constituent of collagen, has two roles in wounded animals. It is essential for the synthesis of increased amounts of reparative collagen required for wound healing, and it decreases some of the negative aspects of the metabolic responses to injury. These are thought to be associated with an arginine-induced growth hormone release.

It is now recognized that successful wound healing is dependent upon an adequate supply of critical nutrients, notably proteins such as collagen, amino acids and other specific vitamins and minerals. In the absence of these nutrients or when the supply is inadequate, wound healing is delayed or compromised. The amino acids found in collagen are critical components in fibroblast formation, collagen synthesis, wound contraction and scar formation. In a study conducted by Irvin[42] in malnourished rats, it was determined that rats given oral supplements of amino acids had an associated significant improvement in the tensile strength and collagen content of abdominal wounds. There was a profound improvement in wound healing for those animals given the amino acids.

There is supporting documentation[43] that indicates the oral consumption of dietary peptides (i.e. hydrolyzed protein) cross the small intestine and reach peripheral tissue via the systemic circulation. Dietary peptides can have specific actions on the gastointestinal tract or at more distant sites. These bioactive peptides can alter cellular metabolism and may act as vasoregulators, growth factors, releasing hormones, or neurotransmitters. The concept of dietary bioactive peptides offers an explanation for varying effects of diet on physiologic responses.

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