A Rationale for the Use of Glandular Products

By Robert Ronzio, Ph.D.

Introduction: *Glandular therapy, or organotherapy, refers to the use of specific animal tissues and cell preparations to improve physiologic functioning and to support the natural healing process. In the 1930's, when glandular use in clinical practice was commonplace, physicians such as Henry Harrower, M.D., W. Powell Cortrille, D.O., Francis Pottenger, M.D. and Royal Lee, D.D.S. emphasized the importance of supplementation with glandulars.*

During the 1940's and 1950's, with the advent of antibiotics and the isolation of vitamins and hormones, glandulars lost favor in the American medical community. Recent research provides a foundation for understanding mechanisms of action and an impetus for the growing interest in the use of glandular products in nutritional protocols. Several reviews have described the rationale and use of glandular preparations.[1, 2, 3, 4, 5]

While different companies have employed various methods and materials to produce glandular materials, Biotics Research Corporation, developed an approach, reflecting a very different perspective.

The development of Biotics Research's glandular products was the offshoot of original research performed by its CDC-licensed, genetics-toxicology testing laboratory in the 1980's. When Biotics Research Corporation developed the first mobile laboratory to respond to environmental contamination requiring a rapid assessment of possible chromosomal damage, fetal calf serum was required to culture of human cells. When the supply of fetal calf serum became limited due to increased demand by biotech firms, Biotics Research had to examine newborn calves as an alternative source. Serum isolated from these animals tested at the National Institutes of Health matched the quality of fetal calf serum. Therefore, using newborn calves as a source of high quality glandular tissues followed naturally from this research. To process these newborn tissues, Biotics Research used low temperature drying and mild solvents to preserve enzymes, proteins and polypeptides, maintaining traits of the original glandular material in as natural a state as possible.

The results of a histological examination of adult and newborn bovine tissues have been published.[6] *This study demonstrated the profound cytological differences between tissues from young calves and those from cattle (the common source of tissue for most preparations), especially pertaining to structural integrity, fatty tissue infiltration and glandular degeneration as a result of aging.*

Whole Glandular Concentrates Provide Multiple Factors

Conventional wisdom ascribes the effects of glandulars to the presence of small amounts of hormones, thus the use of glandulars is often viewed as hormone replacement. In fact, the situation is quite different. Glandular products provide a balance of multiple factors to promote growth and maintenance of organs and glands, rather than an excess (pharmacologic level) of a single hormone or factor.

Preparations from healthy organs can supply substances that may be deficient in the corresponding organ in vivo, including nuclei acids and organ-specific enzymes. Pancreatic enzymes are well documented examples. Glandular products can include certain peptide hormones, such as thymic hormones; neuropeptides of the hypothalamus/pituitary axis; growth and other factors; glycosaminoglycans; glycolipids and phospholipids; enzyme cofactors; mineral storage proteins and other substances.

Insights Regarding the Mechanism of Action of Glandular Products

Scientific advances of the last 20 years can now answer three fundamental questions regarding the efficacy of glandular products.

1) Do glandular products survive the digestive tract, and are they absorbed? In other words, aren't glandulars simply dried meat tablets?

2) If glandular constituents are absorbed orally, what is the evidence for their specific effects on glands and organs?

3) Doesn't the presence of trace levels of well-known hormones explain the actions of glandular products?

Evidence for the absorption and assimilation of glandular peptides and proteins

Proteins, including enzymes such as chymotrypsin, bromelain and amylase, can be absorbed intact.[7,8,9,10] Radioactively tagged pancreatin, papain, lipase, chymotrypsin and bromelain were given to rabbits. The absorbed enzymes were detected in the lung and liver within two hours after oral administration.[11] Absorbed antigens can elicit well-known responses by the gut-associated immune system and generate oral tolerances.[11, 12, 13, 14] Maternal secretory IgA is absorbed by nursing infants up to 4 weeks postpartum.[15] As a further example tritium-labeled thymus extract fed to guinea pigs was incorporated into plasma, liver, kidney and skeletal muscle within 2-8 hours after ingestion.[16] It is estimated that peptides account for 60-70% of luminal nitrogen absorbed by the proximal jejunum.[7]

Approximately 50% of amino aid load from food proteins are absorbed as di- and tripeptides. Furthermore, a variety of biologically active peptides released from protein digestion can be distributed systemically.[17] In calves, approximately 70% of amino acids entering the portal blood were in the form of peptides ranging in molecular weight from 300 to 1500.[18]

Bioactive peptides are readily absorbed and they can reach peripheral tissues and the central nervous system in "active form".[18] Examples of small peptides with marked biological activity include TRH, (3 amino acids), and LHRH, (10 amino acids) and Metenkaphalin (5 amino acids). Zaloga reported that small peptides produced in the diet affect wound healing, cardiovascular and renal function.[20]

Other Possible Bioactive Species in Glandular Preparations

In addition to peptides and polypeptides, glandular preparations may provide organic and inorganic cofactors, and lipid factors that may enhance cellular activity in a particular tissue of the recipient. Among building blocks, phospholipids are essential for cell membrane formation and function. Other lipids can serve as biosynthetic intermediates. As an example, dolichol phosphate is a transporter of glycosyl moieties for glycolipid and glycoprotein synthesis. The contribution of lipid fractions from the pituitary, pancreas, spleens, adrenals, thyroid and gonads to the activity of glandular preparations has been recognized.[21]

Effects of Glandulars On Specific Organs and Glands

Experiments with injected cells or cell constituents that have been chemically labeled suggested these materials can accumulate in target tissues and organs.[22] More than 30 growth factors, peptides and polypeptides have been defined with specific regulatory functions in embryonic development, post-natal growth and maintenance of the adult organs and tissues.[23] Growth factors can be classified according to several families: FGF refers to fibroblast growth factor. FGF is an important antiangiogenic factor, that is, it inhibits the formation of new blood vessels. EFG refers to epidermal growth factor, a polypeptide of 53 amino acids (6,000 mol.wt.). It is produced by platelets, kidneys, intestine and salivary glands.[24] IFG refers to insulin-like growth factors, IFG (somatomedins), which are small proteins mol. wt. about 7,600). IGF-1 and IGF-2 are essential growth factors for cell viability and differentiation. IGF-1 stimulates protein synthesis and tissue regeneration in wound healing .[25] In addition, European researchers provided evidence for endogenous growth inhibitory substances, called chalones, in glands and tissues.[26] Chalones are apparently specific for tissues, not species.[27, 28, 29]

Effectiveness of Lung, Liver and Thyroid Glandulars

A recent study[30] of the effects of raw gland concentrates from liver, lung and thyroid suggested that different glandular preparations exhibit organ specificity. Subjects ingested one of the following for periods lasting from one to four months: bovine liver concentrate (455 mg q.i.d.); or bovine lung tissue concentrate, (180 mg b.i.d.); or porcine thyroid gland concentrate, (160-360 mg per day). Serum ALT was chosen as a marker for liver function; total serum CO2, for lung function, and total serum thyroxin (T4) for thyroid function. Baseline laboratory data were compared with values obtained after supplementation. Of 64 subjects using liver concentrate, 59% showed decreased transaminase levels. In 50 subjects with low initial T4 levels, 76% experienced increased T4 levels. With lung glandular supplementation 43% of 48 subjects showed improvement, while 57% did not improve with supplementation.

Examples of Tissue-specific Factors

Thymic factors. Orally ingested thymic extracts are known to support many aspects of immune function in experimental animals, as well as in humans. Thymic hormones and related cytokines such as interleukins and interferons, control maturation, proliferation, antigen commitment, and cytotoxic activity of various classes of T cells. Most of the reported benefits of thymic extracts have been observed with cellular immunity. Especially thymus extracts stimulated the production, maturation, and activation of T cells.[31, 32] Thymic extracts have been used to restore cellular immunity in secondary T cell immuno deficiencies, for example, in combined immunodeficiency.[33]

Orally administered calf thymus thymomodulin was used with patients with atopic dermatitis, chronic bronchitis, viral infections, recurrent respiratory infection and rheumatoid arthritis.[34] In those patients with low CD4+/CD8+ ratios, the ratio increased significantly. In patients with high CD4+/CD8+ ratios, glandular therapy normalized this ratio.

Orally administered thymomodulin has also been used for children with recurrent respiratory infections.[35] Children with food allergies given oral thymomodulin for 6 months experienced improved food tolerance, with decreased IgE levels.[36] Thymus extract may be effective in restoring a decline in thymic function associated with aging.[32] Pandolfi et al administered thymostimulin to healthy, elderly people.[37] Compared to controls, the supplemented group had significantly lower infections.

Liver. Hepatocyte growth factor is a multifunctional cytokine.[38, 39] Liver extracts have been found to help improve tissue regeneration, fatty acid metabolism and carbohydrate metabolism by the liver and to prevent damage to the liver.[40, 41, 42] In addition, the liver is a rich source of essential nutrients including iron. Heme iron, the naturally chelated form that occurs in tissues, is more readily absorbed than nonheme (plant-derived) iron. Liver is also a source of factors reported to increase endurance in experimental animals.[3]

Hypothalamic factors. Orally administered hypothalamic peptides, such as thyrotropin-releasing hormone (TRH), luteinizing hormone releasing hormone, as well as vasopressin, are significantly absorbed by the gastrointestinal tract. Regarding TRH, the oral route of administration produce a more prolonged stimulation of thyroxine release than when administered intravenously.[43, 44]

Pancreatic function. Pancreatic enzyme supplementation has a long history of use in the medical and nutrition literature.[45] The presence of cofactors such as colipase, a pancreatic peptide, and calcium, which is needed to activate many proteolytic enzymes, enhance the effectiveness of pancreatic enzymes.[45]

Adrenal function. The adrenal medulla produces catecholamines in response to the nervous system. In addition, the medulla secretes enkaphalins, analgesic peptides, together with chromogranin-A, considered an anti stress protein. Bovine adrenal glands contain much more chromogranin than human adult glands.[46] The corticoadrenal glands are critically important for regulating metabolism homeostasis and differentiation. Steroid synthesis in adrenal glands begins in mitochondria and a wide variety of peptides and protein factors regulate the process.[47] Endothelin-1 stimulates enzymes of steroid synthesis in the adrenal cortex, especially mitochondrial membranes and the smooth endoplasmic reticulum.[48]

Spleen function. The spleen represents the largest mass of lymphatic tissue, and in humans it reaches full functional capacity in young adults. The spleen produces unique peptides such as tuftsin, (4 amino acids) and splenopentin (5 amino acids) to enhance immune system. Spleen extracts and splenin, a peptide hormone from spleen, further support the immune system.[49, 50, 51] While Tuftsin stimulates macrophages and other defensive cells[52], deficiency of tuftsin is linked to bacterial infections.[53]

Cartilage and angiogenesis. Cartilage inhibits neovascularization in animal models. Experiments with lab animals indicated that active ingredients of purified cartilage can be absorbed by the intestine and distributed systemically.[54] Prudden has reported the efficacy of bovine cartilage is due to a complex interaction among active principles and aspects of the immune system.[55, 56] Remission of osteoarthritis was observed in 59 percent of patients supplemented with bovine cartilage .[57]

Duodenum. The duodenum produces a wide range of physiologically important peptides and polypeptides. These include somatostatin, epidermal growth factor, secretin, gastrin and cholecystokinin. In addition, growth hormone-releasing factor, usually associated with the hypothalamus, is formed by the duodenum[58] Beta endorphin-like activity has also been reported for duodenum mucosa.[59]

Assessment of the "Morphogen" Hypothesis:

The "Morphogen" hypothesis was developed by Dr. Royal lee and William Hanson in 1947.[60] The authors proposed that genes are organized as units called "cytomorphogens" as distinct from chromosomes. Cytomorphogens were believed to be determinants of cell morphology. "Protomorphogens" were defined as subunits of cytomorphogens, which guide the assembly of functional arrays of individual proteins. Regarding the physical properties of protomorphogens, the authors cited contradictory properties: reportedly it can be stable at temperatures up to 300°C, or it may be inactivated at 60°C. They are absorbed by connective tissue and charcoal. They are either diffusible or nondiffusable; they are extractable by salt solutions, by acetone, ethanol-ether mixtures or nonpolar solvents. It was assumed that extracting raw frozen, ground tissues with high concentration salt solutions selectively extracts nuclear material. However, this procedure does not separate the nucleus from other organelles, and therefore such extracts represent many sub cellular compartments and contain electrolytes, nucleotides, amino acids, trace minerals, bases, enzymes and other soluble proteins, as well as variable amounts of nuclear proteins, and degraded DNA and RNA. Therefore, such an extract is quite heterogeneous.

Critique: There is no modern basis for this outdated model of cell function. Lee and Hanson emphasized inorganic cations in structural organization of cells. However, this association does no confer specificity to nucleic acids. Instead, specificity of cell structure and function is conferred by the amino acid sequences of proteins and the nucleotide sequences of nucleic acids. Chromosomes are composed of DNA condensed around a protein core of histones (the nucleosome), which is the first level of chromatin organization. Nucleosomes self-assemble from DNA and histones in the presence of nucleoplasmin, (an acidic protein that acts as a molecular chaperone to bring histones and DNA), plus DNA topoisomerase.[61] The nucleus exports information to the cytoplasm, as messenger and transfer RNAs. Thus, specificity and organization are controlled by DNA/protein interactions. No details for assaying promorphogens have ever been published. Therefore the nature of such materials cannot be established and quantifying them cannot be performed.

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