

FIRST CALL™ DOUBLE BLIND MEDICAL STUDY

COMPARATIVE STUDY BETWEEN FIRST CALL™, A COMPLEX OF FLAVONOIDS AND POLYPHENOLS CREATED FROM EXTRACTS OF ARTICHOKE AND SARSAPARILLA AND A PLACEBO IN ALCOHOL RELATED LIVER DISEASEAUTHOR SA.

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INTRODUCTION

Currently there is much interest in the health benefits of various phytochemicals. Many of the protective qualities of foods have been attributed to the antioxidant capabilities of such nutrients as the carotenoids, tocopherols, and Vitamin C. Recent research, however, points to a specific group of C15 aromatic plant pigments, called flavonoids, which offer many active principles in medicinal plants. This group of aromatic compounds includes the chalcones, dihydroflavones (flavanones), flavones, isoflavones, biflavonoids, dihydroflavonols, flavonols, anthocyanidins, and proanthocyanidins. Presently there are over 4000 individual flavonoid compounds known.

A single plant may contain several flavonoids with distribution being specific to various parts of the plant. Flavonoids play different roles in each part of the plant. For instance, because of their attractive colors, flavonols, flavones, and anthocyanidins are helpful in signaling pollinating insects. Catechins and other flavonoids have astringent qualities that protect the plant by keeping other insects away. Some flavonoids have UV-absorbing properties and protect the plant from harmful UV radiation from the sun. While others participate in the light phase of plant photosynthesis.

Historically, flavonoids have been described for treating diabetes mellitus, allergy, cancer, viral infections, headache, stomach and duodenal ulcer, liver pathology, and inflammation. They can bind to enzymes, hormone carriers, and DNA; chelate metal ions such as iron, copper, zinc, and manganese; catalyze electron transport; and scavenge free radicals. Most researchers conclude that the pharmacological effect of flavonoids is due to their inhibition of certain enzymes, their metal chelating abilities, and to their antioxidant activity.

FIRST CALL™, originally known, as Liv-1 is a complex of flavonoids and polyphenols created from extracts of the artichoke (*Cynara floridanum*) and sarsaparilla (*Smilax aristolochiaefolia*). It was created by a group of three researchers specializing in pharmacology, plant chemistry, and liver disease. It has been used clinically for almost 30 years in various private medical settings throughout Central and South America with favorable results in addressing many liver and gall bladder disorders. A comprehensive chemical analysis has not been performed at this time. However, a partial analysis for certain flavonoids and polyphenols has been accomplished. This analysis has shown levels of quercetin, kaempferol, isorhamnetin, (+)-catechin, silymarin, cynarin, caffeic acid, and chlorogenic acid.

The artichoke has been used historically in the United States and Europe to treat such conditions as sluggish liver, poor digestion, atherosclerosis, elevated triglycerides and cholesterol, decreased bile secretion, kidney diseases, and proteinuria. In Honduras and Mexico, sarsaparilla is used to treat rheumatism. And in the United States and China, it has been used to treat arthritis, cancer, skin disease, venereal disease, fevers, and digestive disorders. And in one Chinese study, sarsaparilla was found to be 90% effective in treating syphilis.

After years of research with patients in private clinics, it was decided to evaluate this complex (Liv-1) with a randomized double blind placebo study. Patients chosen for this study were those who had been diagnosed with chronic alcoholic liver disease caused by excessive ingestion of alcohol (excessive ingestion being defined as one (1) to one and one half (1 ½) liters of tequila or brandy per day for extended periods of time). The patients were diagnosed and chosen in the Clinic par la Attention de Problemas Relacionados con el Alcohol (CAPRA) at the General Hospital in Mexico City, which belongs to the Secretaria de Salud (Equivalent to the U.S. Department of Health). (Translation: Clinic for the Attention of Problems Related to Alcohol)

METHODOLOGY

The study chosen was a randomized double blind placebo study in which neither the treating physicians in charge or the patients knew to whom the real product or the placebo was administered. Sixty (60) patients were divided in a random way into two (2) groups of thirty (30) each. Of these sixty test subjects, 53 were male and 7 were female with ages running from 26 years of age to 52 years of age (average age 37.3 years). All of the patients had tests made of liver performance, hepatic cytology, blood analysis, prothrombin time, urine tests, and clinical examination. These same tests were completed again at the end of the study. The treatment lasted thirty (30) days and each patient took three capsules (420 mgs. each) three times per day.

DEFINITION OF PARAMETERS AND RESULTS EXPRESSED IN PERCENTAGES

To make this report useful and keep misinterpretations to a minimum, it was important that we defined the following clinical parameters, laboratory analysis, and results in a clear and simple way. The following results have been expressed in percent improvement, which was determined using two indices, the Maddrey and Orrego (see references below). Results were measured before and after treatment, calculating the difference, and expressing these results as a percentage of recuperation.

Maddrey, C.; Willis; Boitnott, K.; Bedine, S.; Weber, L.; Fredrick; Mezey, E.; White, R.; Corticosteroid Therapy of Alcoholic Hepatitis. *Gastroenterology* 75: 193-199. 1978.

Orrego, H.; Kalant, H.; Israel, Y.; Blake, J.; Medline, A.; Rankin, J.; Armstrong, A.; Kapur, B.; Effect of Short-Term Therapy with Propylthiouracil in Patients with Alcoholic Liver Disease. *Gastroenterology* 76; 105-115. 1978.

Ascites

Ascites is the effusion and accumulation of serous fluid in the abdominal cavity. It is found commonly in those diagnosed with liver disease. A 72.38% reduction of ascites was observed in the experimental group. The placebo group experienced a 6.35% increase in abdominal fluid.

Encephalopathy

Encephalopathy is a degenerative disease of the brain. Hepatic encephalopathy is a condition usually occurring secondarily to advanced disease of the liver. It is marked by disturbances of consciousness, which may progress to deep coma (hepatic coma), psychiatric changes of varying degree, flapping tremor and fetor hepaticas. It is also referred to as portal-systemic encephalopathy. A 66.08% reduction of encephalopathy was obtained in the experimental group. The placebo group saw a 12.24% increase in these symptoms.

Splenomegaly

Splenomegaly is enlargement of the spleen. Congestive splenomegaly often results from cirrhosis of the liver and is also characterized by anemia and hemorrhages. An 88.40% reduction in spleen enlargement was noted with the treated group. The placebo group worsened by 11.54%.

Hepatomegaly

Hepatomegaly is enlargement of the liver. It is seen as a result of cirrhosis, fatty infiltration, passive congestion, and early biliary obstruction. The treated group experienced a 93.33% reduction in enlarged livers. In the placebo group their livers continued to enlarge by another 7.14%.

Weakness

Weakness is defined as lacking physical strength or vigor, asthenia, atony, cardiasthenia, fatigue, and lassitude. The treated group noted a 73.64% increase in strength. There was a decrease in muscle strength in muscle strength by 7.41% in the placebo group.

Peripheral Edema

Peripheral edema is a condition in which the peripherals body tissues contain an excessive amount of tissue fluid. It results from increased permeability of the capillary walls due to possible disturbances in renal functioning, reduction of plasma proteins, fluid and electrolyte imbalances, and malnutrition. Edema in the extremities of the treated patients decreased by 48.21% in the treated group. There was no change in the placebo group.

Hemorrhages

Hemorrhaging is bleeding. Many alcoholics present with massive upper GI bleeding from esophageal varices secondary to portal hypertension (increased pressure in the portal vein as a result of obstruction of the flow of blood through the liver). The treated group noted a 100.00% decrease in capillary hemorrhaging in the skin, gums, and nasal membranes. The placebo group saw an increase of 28.57% in hemorrhaging.

Anorexia

Anorexia is defined as loss of appetite. Anorexia is seen in depression, malaise, commencement of fevers and illness, also in disorders of the alimentary tract, especially the stomach, and as a result of alcoholic excesses, drug addiction or certain medicines. Anorexia decreased in the treated group by 76.98%. The placebo group noted a decrease of 3.70%.

Abdominal Wall Veins

Abdominal Wall Veins are very tortuous (having many twists or turns) veins visible throughout the abdomen of the patient. Related to ascites. The experimental group saw a 60.62% reduction while the placebo group experienced a 3.33% reduction.

Palmar Erythema

Palmar erythema is reddish and swollen palms due to muscular hypotrophy (progressive degeneration and functional loss of cells and tissues). The Liv-1 group experienced a 26.67%% reduction in palmar erythema and there was no change with the placebo group.

Telangiectasia

Telangiectasia is a vascular lesion formed by dilatation of a group of small blood vessels of the skin. The Liv-1 group saw 60.00%% reduction in these lesions. While in the placebo group there was a 3.33% reduction.Total

Bilirubin

Bilirubin is the predominant pigment of human bile and it gives the bile a golden yellow color. Total serum bilirubin may be increased in cirrhosis of the liver and acute viral hepatitis. The experimental (Liv-1) group saw a 38.95% reduction in total bilirubin and the placebo group saw a 5.68% increase.

Alkaline Phosphatase

Alkaline phosphatase is an enzyme that hydrolyzes monophosphoric esters liberating inorganic phosphate. Its optimum pH is about 9.0 (alkaline) and functions in the mineralization process of bone. It is excreted by the liver; hence its levels increase in the blood whenever an obstructive liver condition exists. Patients taking the Liv-1 obtained a 25.91% reduction in alkaline phosphatase blood levels and the placebo group saw an increase of 11.69%.

Serum Glutamic Oxaloacetic Transaminase (SGOT)

Oxalacetic glutamic transaminase is an enzyme distributed throughout all tissues, but especially found in high concentrations in the heart and liver. OGT is increased in cases of hepatitis, hepatic necrosis, cirrhosis, and hepatic metastasis. SGOT is now more commonly referred to as aspartate aminotransferase. The treated group noted a decrease of 23.83% in SGOT levels. The placebo group experienced a worsening of 11.71%.

Prothrombin Time

Prothrombin time is a test of clotting time made by determining the time for clotting to occur after thromboplastin and calcium are added to decalcified plasma. There was a decrease in prothrombin time in the experimental group of 42.00%. An increase in clotting time was noted in the placebo group of 6.60%.

Serum Albumin

Serum albumin is one of a group of simple proteins widely distributed in tissues; it is found in the blood. Low levels of albumin in blood plasma are associated with a pathologic condition of the liver. The experimental group saw an increase in serum albumin of 37.27%. There was a decrease in the placebo group of 1.95%. Gamma Glutamyl Transpeptidase (GGT) GGT is a tissue enzyme that is elevated in many conditions involving hepatic damage including, alcohol-induced hepatic injury; in patients with renal disease, pancreatitis, diabetes mellitus, and coronary artery disease. The treated group noted a reduction of 23.79% in GGT. The placebo group experienced an increase of 9.92%.