

## Preliminary Evaluation of a Nutraceutical Product Made with Residue of *Cocos Nucifera* for Use in the Treatment of Obesity

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### Abstract

In recent years, agro-industrial residues of plant or vegetal origin have been shown to be a useful source of fiber and antioxidant components. Both types of elements have beneficial effects on human health. *Cocos nucifera* is abundant in tropical and subtropical countries, and up to 50% of its fruit is considered non-industrializable residue. There is sufficient previous evidence to think that the use of this residue in the manufacture of nutraceutical products may have beneficial effects on weight gain in obese individuals. Therefore, the present study evaluated the toxicological risk of an extract obtained from *C. nucifera* residue as well as the effectiveness of a nutraceutical product made with this extract, on weight gain in mice with diet-induced hypercholesterolemia. Our results show reduced weight gain and glucose levels in mice administered the nutraceutical product made with coconut residue extract. This study shows that coconut residue extract is a suitable alternative for obesity control, but further evaluation is needed of other biochemical markers of anti-obesogenic effect to ensure the effectiveness of the nutraceutical product for human consumption.

Keywords: Obesity; Metabolic syndrome; Coconut; *Cocos nucifera*; Residues food

Abbreviations: N: Negative; H: Positive control; NP: Base Nutraceutical Product; NPC: Nutraceutical Product made with Coconut Residue Extract

### Introduction

There is growing interest today in the use of agro-industrial residues of plant and vegetal origin since they are increasingly valued as an alternative source of phytochemical compounds of industrial importance [1,2].

In *Cocos nucifera*, the coconut palm abundant in tropical and subtropical countries such as the Philippines, Malaysia, India and Mexico, some 40 to 50% of the components [3]. Since dietary fiber plays an important role in human health, high fiber diets have proved to have beneficial effects on human nutrition due to their potential application for weight control [4] and prevention of chronic degenerative diseases such as cancer, cardiovascular disorders and diabetes mellitus [5]. Also, antioxidants present in this type of fruit can reduce the oxidative damage induced by free radicals on biomolecules [6].

For the past two decades, research on nutrition has focused on both nutritional and non-nutritional components as well as their respective role in disease prevention [7]. This has brought about an increase in the market for nutraceutical products and functional foods, giving an impulse to the study of alternative natural sources of antioxidants.

To establish whether a nutraceutical product or functional food will in fact improve a specific health aspect, the bioavailability, effectiveness and safety of the product must be determined [8,7]. Thus, the present study evaluated the toxicological risk of an extract obtained from *C. nucifera* residue, as well as the effectiveness of a nutraceutical product

made with this extract on weight gain in mice with diet-induced hypercholesterolemia.

### Materials and Methods

#### Animals

Male and female CD1/ICR mice were purchased from PROPECUA. Specimens used in the study were cared for and maintained as provided by Mexican regulation (NOM-62-ZOO-1999) on the care, maintenance and use of laboratory animals. Briefly, mice were lodged in polycarbonate rodent cages (4 per cage) in a climate-controlled room at 22°C ± 2°C, with 50% relative humidity and light/dark cycles, with light on at 8:00 am. Specimens were acclimated for seven days prior to use. Unless otherwise stated, during this period and throughout the experiment water and food were provided ad libitum.

#### Preparation of the extract of *C nucifera* residue

A total of 15 mL of 80% ethanol were added per gram of dry sample. The mixture was allowed to macerate for three days. The volume was then reduced to eliminate the solvent by rotary evaporation at 55°C and reduced pressure.

#### Evaluation of extract toxicity

The acute toxicity assay was performed according to Annex 2a of OECD Guideline 423 for the testing of acute oral toxicity. Male and

female mice (n=3 respectively) maintained as described at the beginning of this section, were administered a dose of 2,000 mg/kg of the coconut residue extract dissolved in water at 10 mL/kg, via intragastric tube, after which, specimens were observed at least once every 30 min for the first 4 h, and thereafter each hour up to 24 h, followed by daily observation every 12 h for the next 14 days. During this period, the behavior of each specimen was recorded and careful monitoring was made of signs of possible toxicity, in particular specimen mortality, tremors, salivation, convulsions, lethargy and somnolence. Body weight was recorded at the start of the study and then weekly up to its end. After 14 days, specimens were weighed, humanely sacrificed, and a necropsy was performed, removing the main organs (brain, heart, liver, lungs, pancreas, spleen, kidneys and stomach). Using the mortality index obtained in this assay, the evaluation was repeated on two other batches of male and female mice (n=3 respectively) administering the same dose under similar conditions. With the results of these two evaluations, and taking into account pertinent literature as well as considerations in Annex 2a of OECD Guideline 423, the toxicity of the extract was determined as to risk category.

### Preparation of a nutraceutical product by adding coconut residue extract

Table 1 lists the formulation of ciabatta bread made with coconut residue extract (as a substitute for 5% of the white flour).

Ingredients	Ciabatta without substitution (Np)	Ciabatta W/ 5.0% Substitution (NPC)
Wheat flour (g)	500	475 g
Yeast (g)	5	5
Honey (g)	9.3	9.3
Salt (g)	10	10
Water (mL)	375	237.5
Extract (mL)	--	137.5

**Table 1:** Formulation of ciabatta bread made with coconut residue extract as a substitute for 5% of the white flour.

Evaluation of the effect of administration of the nutraceutical product made with coconut residue extract

Male ICR mice weighing 25-30 g were acclimated as described at the beginning of this section for one week prior to the assay. To induce hypercholesterolemia, a diet consisting in 1% cholesterol, 5.0% butter, 0.5% sodium cholate, 30% powdered sugar, 10% lactic casein and 53.5% standard rodent food (Rodent Lab Chow) was provided ad libitum throughout the study. Another group of mice was fed a normal rodent diet. Mice receiving the base nutraceutical product without coconut residue extract (NP) or the nutraceutical product with this extract (NPC) were administered these foods via intragastric tube.

Mice were distributed at random into six groups (n=10): (1) negative control (N), were provided a standard rodent diet and were administered the vehicle via intragastric tube; (2) positive control (H), were fed a hypercholesterolemic diet and were administered the vehicle intragastrically; (3) base nutraceutical product (NP1) in a 420 mg/kg

dose; (4) base nutraceutical product (NP2) in a 1,280 mg/kg dose; (5) nutraceutical product made with coconut residue extract (NPC1) in a 420 mg/kg dose; and (6) nutraceutical product made with coconut residue extract (NPC2) in a 1,280 mg/kg dose. Groups 2 to 6 were provided the hypercholesterolemic diet ad libitum.

These treatments were administered for 4 weeks. Body weight was recorded at the start of treatment and weekly thereafter. At the end of this period, mice were made to fast for 12 h, blood samples were taken, the serum was separated and glucose levels were quantified using a glucometer.

## Results

### Evaluation of toxicity

During the 14 days subsequent to administration of the extract, no mortality events occurred in either males or females. Similarly, no changes in physical appearance were observed: normal coat shine and new growth unchanged; pink coloration of nose, ears, paws and tail; and oral cavity mucosa and eyes well hydrated. The gait, preening and exploratory behavior proper of this strain were maintained. Since the same results were obtained in duplicate and there is no evidence of acute toxicity of extracts derived from the shell as opposed to the flesh or milk of *C. nucifera*, the extract was classified as Category 5 in terms of acute toxicity.

### Preparation of a nutraceutical product by adding coconut residue extract

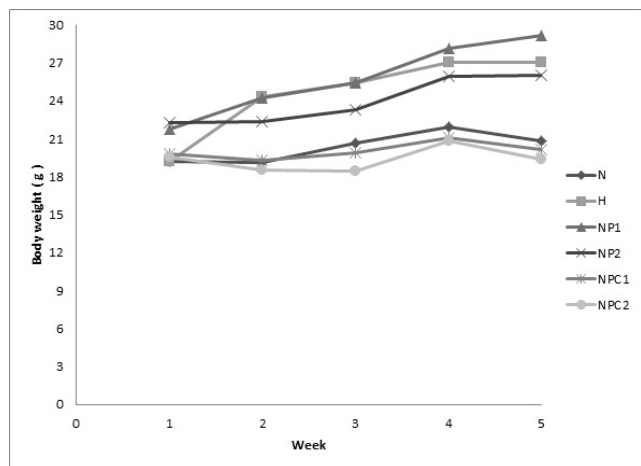
Ciabatta is an oven-baked bread with a crispy outer layer and a well honeycombed crumb due to the high hydration of its dough. The batch made by substituting 5% of the white flour with coconut residue extract resulted in a product with bread-like characteristics (Table 2).

Characteristics	Control ciabatta (NP)	Ciabatta with 5% coconut residue extract (NPC)
Weight (g)	32.18 ± 1.7029	21.266 ± 4.1324
Volume (mL)	175 ± 30.2765	145.2 ± 9.5236
Texture (kgf)	0.7 ± 0.1154	4.2 ± 1.0954
Crust color index	2.9957 ± 0.8	3.1715 ± 0.1
Crust color	Pale yellow	Beige
Crumb color index	2.9981 ± 1.7015	5.3867 ± 3.9091
Crumb color	Pale yellow	Beige

**Table 2:** Bread quality characteristics of control ciabatta and ciabatta made with coconut residue extract substituting 5% of the white flour.

Evaluation of the effect of administration of the nutraceutical product made with coconut residue extract.

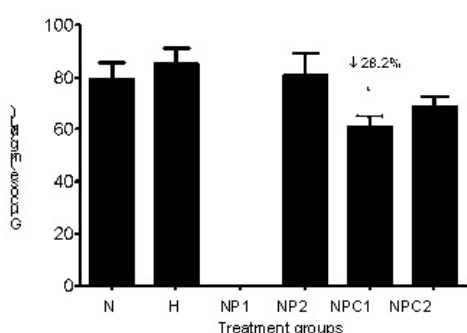
Figure 1 shows body weight variation in mouse groups throughout the four weeks of treatment.



**Figure 1:** Effect of administration of a nutraceutical product on body weight variation in male mice with diet-induced hypercholesterolemia. N = negative control; H = positive control; NP1, NP2 = nutraceutical product without coconut residue extract (1: dose 0.42 mg/kg; 2: dose 1.28 mg/kg); NPC1, NPC2 = nutraceutical product with coconut residue extract (1: dose 0.42 mg/kg; 2: dose 1.28 mg/kg).

A statistically significant weight reduction is observed with respect to the positive control in mice administered either dose of NPC, while no difference is seen with respect to the negative control. On the other hand, mice administered either dose of NP showed no differences with respect to the positive control.

As regards blood glucose levels, Figure 2 shows that the 420 mg/kg dose of NPC induced a significant decrease with respect to the positive control.



**Figure 2:** Effect of administration of a nutraceutical product on blood glucose levels in male mice with diet-induced hypercholesterolemia. N = negative control; H = positive control; NP1, NP2 = nutraceutical product without coconut residue extract (1: dose 0.42 mg/kg; 2: dose 1.28 mg/kg); NPC1, NPC2 = nutraceutical product with coconut residue extract (1: dose 0.42 mg/kg; 2: dose 1.28 mg/kg).

## Discussion

Thanks to recent advances in medicine and biotechnology, human health has plausibly improved, as reflected by the current increase in life expectancy. In many ways, the explosion in food industrialization has had an impact on the incidence of eating disorders such as obesity and metabolic syndrome, which are undoubtedly factors in the development of chronic degenerative diseases (cancer, diabetes and severe vascular disorders among others) and their complications, particularly since such complications have become more frequent and severe due to the higher life expectancy today, the drastic change in eating habits due to food industrialization, and increased sedentariness.

Therefore, government health agencies and consumers are increasingly interested in foods that offer significant health benefits including the so-called functional foods and food supplements referred to as nutraceutical products. These products have been defined as foods, or parts of foods, that are beneficial for disease prevention or treatment [9]. However, both functional foods and nutraceutical products should be used cautiously since major considerations must be taken into account including: the conditions of stability of bioactive ingredients, whether these ingredients are present in sufficient quantity and strength to effectively influence a specific health aspect and, unavoidably, the safety of the components [8,9]. Therefore, in the present study, the safety of the coconut residue extract was determined by evaluating its acute toxicity. The extract was found to correspond to a very low, almost harmless, risk category, which is the category recommended for products that will be incorporated into the human diet.

Coconut products have proved to have diverse beneficial effects on human health such as: being a source of electrolytes, having antioxidant activity, and having anti-thrombotic, anti-atherosclerotic, anticholesterolemic, antibacterial, antiviral, antifungal, immunostimulant, anti-diabetic and hepatoprotective properties [3]. Some of these effects, e.g. anti-diabetic and antioxidant properties, are attributable to the fiber and phenolic compounds present in these products.

A large number of bioactive compounds are generally present in food residues, the main ones being: (1)  $\gamma$ -oryzanol, a potent antioxidant that lowers blood cholesterol levels; (2)  $\beta$ -glucans, which reduce glycemic index values and plasma cholesterol; (3) lignans, which are attributed anticarcinogenic, antioxidant, antibacterial, antiviral and anti-inflammatory effects; and (4) phenolic compounds, which are antioxidants that prevent the damage induced by free radicals and are active in the treatment of cancer and cardiovascular diseases [1].

No evidence has been published to date regarding the presence of phytochemical components in residue of *C. nucifera*, or their bioactivity.

The present study is the first to show that administration of a nutraceutical product made with coconut residue extract to mice subjected to a hypercholesterolemic, hypercaloric dietary regimen significantly reduces weight gain with a parallel drop in serum glucose levels, an effect that may partly be due to the high fiber content in coconut residue [10].

Vegetal fiber from diverse fruit and vegetable sources plays a major role in human health, particularly because of its potential ability to control weight gain, as well as its hypoglycemic effect [4]. Vegetal fiber is not digested in the small intestine but is fermented in the colon,

forming short-chain fatty acids such as acetate, propionate and butyrate. This reduces water absorption in the colon and prevents constipation. Propionate also inhibits the activity of HMG-CoA reductase, a key rate-limiting enzyme for cholesterol synthesis, while fiber prevents resorption of bile acids in the liver inhibiting in turn cholesterol synthesis [5]. This way, lipid metabolism becomes more efficient, avoiding excess accumulation of adipose tissue, with consequent body weight regulation [11]. To all this should be added the fact that the content of phenolic compounds present in *C. nucifera* [12] may contribute to its antioxidant and anti-obesogenic effects. Flavonoids have numerous beneficial effects, including control of de novo lipogenesis, lipogenic inhibition and an increase in the levels of lipolytic enzymes. In C57BL mice with diet-induced obesity, phenolic compounds improved glucose metabolism, reduced the accumulation of lipids in liver and decreased TNF- $\alpha$  levels [13]. In conclusion, the present study shows that the extract obtained from coconut residue, and its derivatives, constitute a suitable alternative for obesity control. However, further evaluation of other biochemical markers of anti-obesogenic effect is necessary to ensure that the nutraceutical product made with coconut residue extract is in fact effective for human consumption.

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