1. **Safety Evaluation in Healthy Colombian Volunteers of P2Et Extract Obtained from *Caesalpinia Spinosa*: Design 3+3 Phase I Clinical Trial**

**Global Use of Natural Products in Cancer Patient Management**

**Background:** The P2Et extract derived from *Caesalpinia spinosa* had antitumor and immunomodulatory activity reported in breast cancer, leukemia and melanoma. In healthy mice was observed that P2Et modulates immune response. Protective effects have been reported in healthy humans, but they could have risk of toxicity.

**Aim:** To evaluate the safety and maximum tolerated dose (MDT) of P2Et extract in Colombian healthy volunteers.

**Methodology:** Phase 1 clinical trial, open labelled, single arm, dose-escalation design 3 +3 study. It was conducted in clinical research center from Hospital Universitario San Ignacio (Bogota, Colombia). Healthy volunteers were included who met the key eligibility criteria, over 18 years old, without multi-organic dysfunction, use of phytomedicines, history of substance abuse or smokers. P2Et extract was administrated in capsules of 600 mg orally daily during 28 days according to dosage level. Adverse events (AEs) were evaluated based on the National Institute of Health Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 and general measurements of health status were performed.

**Results:** MDT for P2Et extract was 600 mg dose, AEs most frequency were gastrointestinal without significant changes in clinical parameters assessed.

**Analysis:** The trial and inform consent form was approved by Hospital San Ignacio independent ethics committee and regulatory authority INVIMA. Trial was registered in clinical trial No. NCT03663881. Analysis by intention to treat was performed, data were expressed as mean (± SE) and median (ranges) with percentage of change between baseline and end visit.

**Results:** 7 healthy volunteer subjects were enrolled. Median of age was 33 years; adherence was 100% in subjects who completed level 1 dosage. There were no severe adverse events, 94.6% of AE were grade 1, and AE less frequent than 5% like adynamia, asthenia, constipation, odynophagia, reflux and viral rhinopharyngitis, most of AE had a reasonable possibility of relationship with study product (83.8%).

**Conclusions:** Oral administration of P2Et extract was safe in healthy humans with a maximum tolerated dose of 600 mg. There was no severe toxicity, most of AE were mild, without significant changes in the safety parameters evaluated.

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