**4.1. Study Design**

**4.1.a. Detail Description**

 **Study Design:** **Title:** American Ginseng and Panaxynol for Ulcerative Colitis: A Clinical and Preclinical Investigation

**Hypothesis:** AG surpasses the suppressive effects of mesalamine on inflammation and disease activity in patients with UC.

**Objective:** To evaluate the potential of AG in suppressing disease activity and inflammation in UC patients undergoing mesalamine maintenance therapy.

**Study Duration:** 6 months (24 weeks)

**Participants:** 60 participants randomly assigned to receive either 3g of AG or placebo.

**Study Design:**

* Double-blind, randomized, placebo-controlled design.
* One intervention period of 24 weeks.

**Inclusion Criteria:**

* Age ≥18 years.
* Active UC with mUCDAI >3.
* On mesalamine maintenance therapy.

**Exclusion Criteria:**

* Targeted immunotherapy.
* Crohn’s disease or indeterminate colitis.
* Positive pregnancy tests or breastfeeding.
* Active infections, malignancies, or investigational drug use.
* Allergies to Ginseng.

**Endpoints:**

1. Primary Endpoint: Clinical Remission
2. Secondary Endpoints:
	* Steroid-free clinical remission
	* Clinical response
	* Endoscopic response/remission
	* Serum biomarkers of colonic and systemic inflammation
		+ Fecal biomarkers: Calprotectin
		+ Mucosal biomarkers: H&E, iNOS, Cox2, Nf-kB
		+ Serum biomarkers: Cytokine profiling (TNF-α, IL-1β, 4, 6, 10, C-reactive protein)
		+ 16S microbiota sequencing of mucosal and fecal RNA

**Study Procedure:**

1. Initial assessments (baseline): mUCDAI, colonoscopy with biopsies, blood, and fecal sample collection.
2. Follow-ups at weeks 4, 8, 12, 16, and 24 to track disease activity.
3. Monitoring flare-ups closely.

**Data Collection:**

* Anthropometrics, vital signs, colonoscopy results, blood, and urine samples.
* Disease Activity Index, C-reactive protein, cytokines, 16S microbiota sequencing.
* Histological assessment, immunohistochemistry, fecal biomarkers.

**Compliance Monitoring:**

* Plasma measurement of Rb1, Rg3, Rg5, and panaxynol.
* Compliance measured through collaboration with the USC Mass Spectrometry facility.

**Statistical Analysis:**

* Within-group and between-group comparisons using analysis of variance and posthoc tests.
* Continuous variables expressed as mean±SD or median.
* Categorical variables expressed as percentages.
* Statistical significance set at p<0.05.

**Expected Results:**

* Anticipate tangible anti-inflammatory impact based on extensive pre-clinical data.
* Ongoing monitoring of bioavailability to correlate with observed outcomes.
* Prepared to explore higher doses in case of minimal differences