PURETRIM FINAL REPORT

The Efficacy And Safety Of Experience®

For The Treatment Of Constipation:

A Randomized, Double-Blind, Placebo-Controlled Trial

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1.0 INTRODUCTION

1.1. Objectives

To provide data regarding the regularity benefits of Experience® in a randomized, double-blind, placebo-controlled study.

1.2 Background Information

Constipation, defined as the difficult or infrequent passage of feces, is a common condition affecting millions of people of all ages. A wide variety of complaints are associated with constipation ranging from mild indigestion and gas, to serious health problems such as diverticula and hemorrhoids resulting from the high pressures exerted during defecation.

2.0 METHODS

This study was a randomized, double-blind, placebo-controlled trial in which 14 men and women, with chronic constipation [(>/= 3 months) defined as </=3 bowel movements per week in the absence of a laxative treatment, or laxative required to maintain >/= 3 bowel movements per week] were randomly assigned to receive Experience® (n=7) or placebo (n=7) during a 3 week treatment period.

2.1 Ethics

This study was conducted according to Good Clinical Practice, the Declaration of Helsinki, and US 21 CFR Part 50 - Protection of Human Subjects, and Part 56 – Institutional Review Boards. A signed written informed consent was obtained from each subject prior to any protocol-specific study procedures being carried out.

2.2 Test Product and Placebo

Experience® is an organic recipe that contains a proprietary blend of psyllium seed husk, rhubarb root, fennel seed, corn silk, King Solomon seed, and kelp. The placebo was formulated and packaged to appear identical to the test product.

2.3 Dose and Mode of Administration

Subjects were instructed at the baseline visit to take 1 capsule of Experience® or placebo with 2 glasses of water before going to sleep at night for days I to 3. On days 4 to 6 they were instructed to take 2 capsules of Experience® or placebo with 2 glasses of water before going to sleep at night. From days 7 to 21 they were instructed to take 3 capsules of Experience® or placebo with 2 glasses of water before going to sleep at night.

2.4 Safety Evaluation

Vital signs and body weight were measured at each clinic visit. Laboratory analyses including hematology,

urinalysis, and serum chemistry were conducted at screening and following three weeks of treatment with study product.

2.5 Statistical Analyses

This was a double-blind placebo-controlled pilot study designed to examine the effects on regularity and safety variables of an escalating dose of Experience®. The sample included 14 subjects randomized in equal numbers to placebo and Experience® groups (Table 2). Intent-to-treat population (all subjects who received at least one dose of study product) was used for the statistical analyses.

Average number of daily bowel movements were calculated and compared between treatment. Furthermore the change from baseline to days 1 to 6 and from baseline to days 7 to 21 of the treatment period were compared using both forms of statistical analyses and changes within treatment groups were analyzed.

3.0 RESULTS

3.1 Efficacy

3.1.1 Primary Efficacy Variable

In order to incorporate bowel movement data from subjects who dropped prior to the end of the study, the average number of daily bowel movements per subject based on the days in the study were calculated. These data are summarized in Table 5. At baseline (days -3 to 0) placebo and Experience® groups had similar median average bowel movements of 0.67 and 1, respectively. A significant difference between placebo and Experience®-treated subjects was demonstrated at both visits 3 (days I to 6) and 4 (days 7 to 21).

Table 5. Average Bowel Movements at Baseline, Visit 3, and Visit 4 [1,2]

	Placebo	**Experience®**
Baseline		
Mean±SEM	0.67±0.15	1.10 ± 0.34
Median	0.67	1.00
Visit 3		
Mean±SEM	0.68±0.16	1.28±0.12
Median	0.83	1.14
Visit 4		
Mean±SEM	0.89±0.19	1.61 ± 0.24
Median	0.69	1.39

[1] Average bowel movements were calculated as: total number of bowel movements / total number of days that subject received study product during that time period.

[2] Baseline = days -3 to 0, Visit 3 = days 1 to 6, Visit 4 days 7 to 21.

3.1.2 Secondary Efficacy Variables

Subjective measures of regularity benefit were determined from a questionnaire regarding

1) consistency of stool, 2) straining, 3) pain, 4) completeness of evacuation, and 5)overall feeling of constipation. Subjects were asked to rate each of these areas using a scale from 1 to 7 with 1 being "very soft," "none," or "complete" and 7 being "very hard," "extreme," or "incomplete." Responses to the questionnaire for the first bowel movement of every day that a bowel movement was reported were used for the analyses (Table 6). Subjects in both treatment groups had similar responses to all of these questions at baseline (days -3 to 0). Responses to the consistency of stool questions at visit 3 (days 1 to 6) and visit 4 (days 7 to 21) of the treatment period were significantly different between treatment groups. Furthermore within the Experience®- treated group, stool consistency improved (became softer) at visit 3 and visit 4 compared to baseline.

With regards to the straining component of the questionnaire, straining was statistically less in the Experience®-treated group compared to placebo at visit 3 and visit 4. Responses to completeness of evacuation questions were found to be different between treatment groups only at visit 4.

Table 6. Subjective Measures of Constipation at Baseline, Visit 3 and Visit 4

		Placebo	Experience®
Consistency of Stool			
Baseline	Mean ± SEM	5.2 ± 0.5	3.7 ± 0.7
	Median	4.8	4.5
Visit 3	Mean ± SEM	4.1 ± 0.4	2.0 ± 0.4
	Median	3.9	1.9
Visit 4	Mean ± SEM	3.6 ± 0.6	1.6 ± 0.2
	Median	3.4	1.9
Straining			
Baseline	Mean ± SEM	4.3 ± 0.8	2.9 ± 0.7
	Median	4.5	3.0
Visit 3	Mean±SEM	3.7 ± 0.3	1.9 ± 0.4
	Median	3.6	1.9
Visit 4	Mean ± SEM	3.5 ± 0.7	1.3 ± 0.2
	Median	3.0	1.0

Pain		Placebo	Experience®
Baseline	Mean±SEM	2.7 ± 0.7	2.1 ± 0.5
	Median	2.5	2.0
Visit3	Mean±SEM	1.6 ± 0.3	1.5 ± 0.2
	Median	1.4	1.0
Visit 4	Mean ± SEM	1.9 ± 0.4	1.3 ± 0.2
	Median	1.9	1.0
Completeness of Evacuation			
Baseline	Mean ± SEM	4.7 ± 0.7	3.6 ± 0.3
	Median	5.00	4.00
Visit 3	Mean ± SEM	4.2 ± 0.6	3.2 ± 0.5
	Median	3.75	2.88
Visit 4	Mean ± SEM	3.7 ± 0.4	2.6 ± 0.4
	Median	3.65	3.14
Overall Feeling of Constipation			
Baseline	Mean±SEM	3.7±0.4	2.7±0.6
	Median	3.75	2.5
Visit 3	Mean ± SEM	3.5 ± 0.4	2.8 ± 0.5
	Median	3.08	2.71
Visit4	Mean±SEM	3.2±0.3	2.1±0.5

[1]Baseline = days -3 to 0, Visit 3 = days 1 to 6, Visit 4 = days 7 to 21.

3.2 Safety

3.2.1 Laboratory Variables

There were no statistically significant differences in laboratory shifts between placebo or Experience® treated subjects. Laboratory values were within safe limits, and changes were deemed to be clinically insignificant by the Investigator.

3.2.2 Adverse Experiences (AE's)

There were three AE's deemed by the Investigator to be related to the study product.

These included:

- flatulence (n= 1 Experience®)
- abdominal pain (n=l Experience®)
- severe constipation (n=l Placebo)

There were three AE's deemed by the investigator to be probably unrelated to study product.These included:

- dizziness (n=l Experience®)
- flatulence (n = 1 Experience®)
- diarrhea (n = 1 Experience®)

There were two AE' s deemed by the Investigator to be unrelated to study product.

These included:

- influenza (n=l Placebo)
- hemorrhoids (n~2 Placebo)

A total of 3 subjects (n=2 Experience®), n=1 placebo) dropped from the study prior to its completion.The subject in the placebo group withdrew due to severe constipation.The subjects in the Experience® group withdrew due to abdominal cramping and gas, and diarrhea and gas.The diarrhea may have been related to the dose of study product, and could perhaps have been alleviated by lowering the dose of Experience®.

4.0 CONCLUSIONS

The results of this randomized, double-blind, placebo-controlled study suggest that Experience® may provide a regularity benefit to otherwise healthy persons suffering from constipation. One week of treatment with Experience® at a dose of 1 to 2 capsules per day resulted in a significant increase in the average number of bowel movements per day when compared to placebo. Escalation of this dose to 3 capsules per day for an additional two weeks continued to provide a regularity benefit compared to placebo. The study product was generally well-tolerated by subjects. **The results of this study provide support that Experience® is efficacious for the treatment of constipation.**