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Evaluation of Safety and efficacy of dietary fiber supplementary combinationin patients with chronic metabolic disorders (type-2 diabetes mellitus, dyslipidemia, overweight, obesity) and chronic GIT disorders (Constipation and Irritable bowel syndrome) with or without comorbidities for 4-12 weeks in outpatient department: an observational study

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ABSTRACT

Introduction: Intake of dietary fibre (DF) has beneficial effects on the risk factors responsible for development of several chronic diseases like IBS, obesity, colorectal cancer, type 2 diabetes and cardiovascular diseases. Hence this study was conducted with aim to evaluate the safety and efficacy of Fitofy, a soluble dietary supplement in various chronic metabolic disorders and chronic GIT disorders with or without other co-morbidities. **Methodology:** This prospective, observational, multicentric study was conducted for a period of one year from Jan 22 to Dec 22 including 120 patients. **Results and discussion:** Statistically significant improvement was seen in various efficacy parameters such asglycaemic control amongst diabetes mellitus patients and lipid profile in dyslipidaemia. Various efficacy parameters for obesity like weight, hunger level and waist circumference showed highly statistically significant fall from baseline. Significant reduction was observed in stool hardness and sensation of incomplete evacuation parameters in patients with constipation. Spontaneous defecation and bowel frequency per week also showed good improvement.Good to excellent safety was observed in 97.19 % of the patient. No adverse event was reported by physician in any patients, A view of good to excellent tolerability was opined by 84.30 % patients. **Conclusion:** The dietary fiber supplement combination (DFSC) of inulin, partially hydrolysed guar gum, and resistant maltodextrin with proper diet therapy/modifications is found to be safe and effective in causing significant improvements in efficacy parameters of various chronic metabolic disorders like type 2 DM, dyslipidaemia, overweight/obesity, and chronic GI disorders.

Key Words: *dietary fiber supplement combination (DFSC), Chronic metabolic disorders, chronic GIT disorders.*

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INTRODUCTION

Intake of dietary fiber (DF) has beneficial effects on the risk factors responsible for development of several chronic diseases [1]. Prior reviews suggest that it is effective for reducing the incidence of cardiovascular disease, type 2 diabetes, and colorectal cancer [1–3]. However, It's a common practice to prescribe DF supplementation for patients with constipation [4–6]. or gastrointestinal conditions such as irritable bowel syndrome (IBS) or to enhance weight loss in patients being treated for obesity [6].

Dietary Fibers have different physiological effects including laxation, attenuation of blood glucose, and normalization of serum cholesterol levels.

The solubility of dietary has been thought to be linked to cholesterol-lowering effects. Dietary fiber may also reduce postprandial blood glucose levels and may have an effect on insulin sensitivity [1].

Traditionally two basic categories of dietary fibres are used in therapy, soluble and insoluble. Insoluble fibres include Cellulose, hemicellulose and lignin whereas soluble fibre includes pectins, gums and mucilages and form gel like consistency on coming in contact with liquid [7].

Fitofy a dietary fiber supplementary combination (DFSC) contains three soluble fibers that is Resistant maltodextrin, Inulin and Partially hydrolysed guar gum. It forms gel like fiber when comes in contact with fluid and fermented by gastrointestinal bacteria further producing short chain fatty acids (SCFA)

The regulation of luminal pH, formation of mucus, provision of energy for epithelial cells, and impacts on mucosal immune function are all facilitated by microbial SCFA synthesis, which is crucial for gut integrity. A variety of tissue-specific processes linked to hunger regulation, energy expenditure, glucose homeostasis, and immunomodulation are used by SCFA to directly affect host metabolic health. Clinical research data also point to the possibility that boosting SCFA production could be an effective method for reducing obesity, type 2 diabetes, reducing LDL cholesterol levels and gastrointestinal dysfunction [8].

Hence, we have conducted a study to evaluate the safety and efficacy of Fitofy a soluble dietary supplementation in various chronic metabolic disorders and chronic GIT disorders with or without other co-morbidities.

MATERIAL AND METHODS

Study objectives:

Primary objective:

To evaluate the efficacy of Fitofy a dietary fiber supplementary combination (DFSC) **in chronic metabolic disorders** such as type-2 diabetes mellitus, dyslipidemia, overweight, obesity and chronic GIT disorders such as Constipation and Irritable bowel syndrome with or without other co-morbidities.

Secondary objective:

To evaluate the safety & tolerability of fitofy a dietary fiber supplementary combination (DFSC) **in chronic metabolic disorders** such as type-2 diabetes mellitus, dyslipidemia, overweight, obesity and chronic GIT disorders such as Constipation and Irritable bowel syndrome with or without other co-morbidities as per patient and physician perspective

Study design

This prospective, observational, multicentric study was conducted for a period of one year from Jan 22 to Dec 22 after getting approval from Institutional ethics committee.

Patients willing to give consent for participation, with more than 15 years of age, either genders, suffering from type-2 diabetes mellitus (T2DM) or dyslipidemia or overweight or obesity or chronic constipation or irritable bowel syndrome and/or co-morbidities and taking dietary soluble fiber composition (Fitofy, Nucgnex Lifesciences Private Limited, Pune, India) as prescribed by physician were included in the study.

Patients having hypersensitivity to any component of the formulation were excluded from the study.

Procedure

Data from total 120 patients included in the study were recorded in the patients proforma. Dietary soluble fiber composition (DFSC) (Fitofy, Nucgnex Lifesciences Private Limited, Pune, India) and its compositions are shown in Table 1.

Table 1: Composition of dietary fiber supplemental combination

Nutrients (Unit)	Per 100 g	Per serving (6 g)
Energy (kcal)	209	12.5
Protein (g)	0	0
Fat (g)	0.1	0.006
Total carbohydrate(g)	92	5.52
Sugar (sucrose)*(g)	0	0
Soluble dietary fiber(g)	80	4.8
***No added sugar (natural sugar may come from other ingredients added)**		

The following dosages of DFSC powder were followed as prescribed by physician: Obese or overweight patients, 6 g DFSC/day for 12 weeks, Diabetes mellitus with/without co-morbidities 6 g DFSC/three times /day for 12 weeks, Dyslipidemia 6 g DFSC/three times /day for 12 weeks, chronic constipation 6 g DFSC/ day for 4 weeks, Irritable bowel syndrome 6 g DFSC/day for 12 weeks.

Administration of DFSC powder: As advised dosage of DFSC powder (one full scoop, 6-8 g approximately) was mixed in 250-300 mL water and consume once or thrice daily (15-20 minutes before meals either pre-lunch, pre-dinner and 30 minutes pre-bedtime) for 4-12 consecutive weeks. Approximately 80% of patients consumed DFSC powder with water with no added sugar, and approximately 20% of patients consumed it with buttermilk with no added sugar.

Dietary Pattern

Most of the patients were following diet patterns before and during the study period.

Before study period: Diet contained 60%- 70% carbohydrate, 8%-12% protein, and 25%-30% fat, with 30 g visible fat/day and less fiber intake.

During the study period: Diet contained 45%-55% carbohydrate, 15%-20% protein, and 20%-25% fat, with 15 g visible fat/day. Calories consumed were 1500-1800 kcal/day on weekdays and approximately 2000 kcal/day on weekends 4- 12 weeks in all patients. All patients were given standard advice regarding healthy food choices in their diet and physical activity. There was vigorous diet monitoring fortnightly for 12 weeks, and a reduction of 200 kcal/day consumption in the diet was decided on a case-to-case basis if needed by reviewing the calorie consumption by every patient. No other nutrient supplementation or weight-reducing medicines were consumed by any patient during 12 weeks of fiber therapy.

Physical activity : All patients had undergone the following physical activity-related interventions: brisk walking for 30-45 minutes a day for three days in a week and either aerobic exercise, e.g., cardiac exercise/high-intensity exercise (an exercise strategy alternating short periods of anaerobic exercise with less-intense recovery periods until too exhausted to continue, e.g., push-ups, sit-ups, lunges, crunches, and running), or resistant training for 30-45 minutes a day for three days in a week during the study duration. The pattern of physical activity for all patients was similar before and during the study.

Follow-up

Observation of Cases

120 patients were included in the study from six centers. Data for each patient was entered in the excel sheet.

Study Visits

The following visits were considered to assess efficacy parameters.

In patients of diabetes mellitus, Dyslipidemia & Irritable bowel syndrome: the First visit, screening day/baseline visit (Day 0) followed by Second visit, at the end of four weeks (Day 28), Third visit, at the end of eight weeks (Day 56) and fourth visit, at the end of 12 weeks (Day 84).

In patients of chronic constipation: the First visit, screening day/baseline visit (Day 0) followed by Second visit, at the end of 1^{st} week (Day 7), Third visit, at the end of 2^{nd} weeks (Day 14), fourth visit, at the end of 3^{rd} weeks (Day 21) and 5^{th} visit was at the end of 4^{th} weeks (Day 28)

In patients of overweight/obesity: 1st visit - Screening day/Baseline visit (Day 0) -2nd visit - after 1 week (Day 7) - 3rd visit -after 4 weeks (Day 28) - 4th visit - after 8 weeks (Day 56) - 5th visit - after 12 weeks (Day 84).
As mentioned before, there was vigorous diet monitoring fortnightly for 12 weeks.

Efficacy parameters: The following parameters were assessed:
In Type-2 diabetes mellitus: Fasting blood glucose,post prandial blood glucose, Glycated Hb (HbA1c).
In Dyslipidemia: Low-density lipoprotein (LDL-c), High-density lipoprotein (HDL-c), Serum triacylglycerol (TG), Total plasma cholesterol.

In Overweight or obesity: Body Weight in Kg, BMI, Waist circumference in cm, Visceral fat area in cm2, Hunger Level Scale (5 rating scale), Calorie/Energy intake (k cal/24 hrs)

In chronic constipation: Stool frequency in a week, Hardness of stool (5 rating scale), Bowel movements with straining (5 rating scale)

Concomitant medication: If any concomitant medication was given to the patient, the same was recorded. Six, one, and two patients were on hypoglycemic, antihypertensive, and anti-hypercholesterolemic medications, respectively body weight (BW) in kg and body mass index (BMI). BMI is calculated by dividing an individual's weight in kilograms by square height in meters.

Safety assessment: Patients were evaluated for their safety based on patients' opinions on the tolerability of the DFSC powder and healthcare professionals' opinions on the safety of the DFSC powder.

Concomitant medication: If any concomitant medication was given to the patient, the same was recorded. Six, one, and two patients were on hypoglycemic, antihypertensive, and anti-hypercholesterolemic medications, respectively.

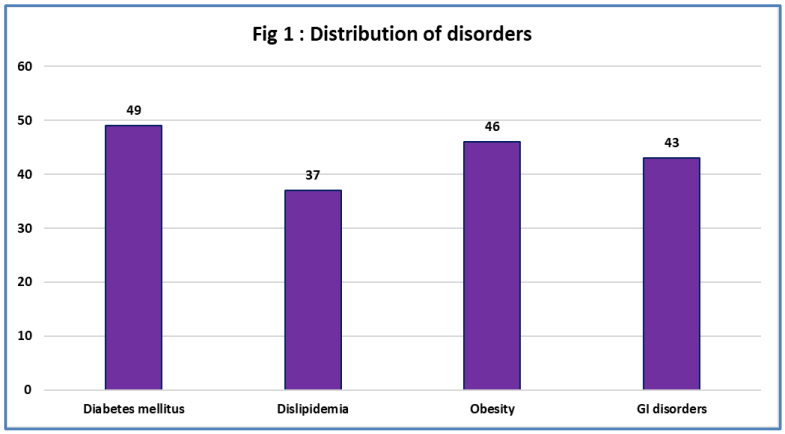
Statistical analysis: The statistical analysis of 120 participants was carried out using the statistical software SPSS version 10.0. The descriptive analysis of demographics and the Student's t-test of significance were used.

RESULTS

Table 2: Demographic data

Total number of patients N (%)	120(100%)
Female	59(49.15%)
Male	61(50.84%)
Age (Mean {SD}) years	45.61(14.7)
BMI (Mean {SD}) Kg/m2	28.93(4.16)
BMI: Body Mass Index	

As shown in table 2, almost equal gender distribution was seen with 45.61(14.7) years mean age and 28.93(4.16) BMI indicating overweight category.



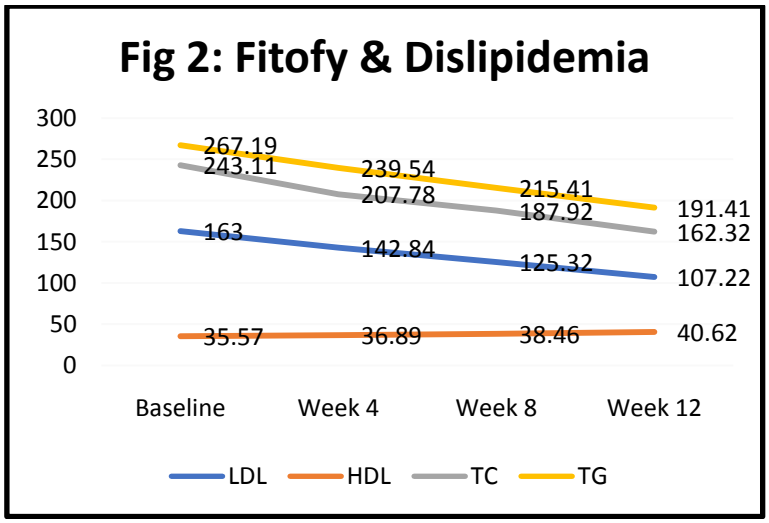
As shown in fig.1, Disorder distribution (patients had single or multiple disorders) has almost equal distribution of various disorders as seen in study subjects. Diabetes Mellitus (49) was the most common disorder followed by obesity (46), GIdisorder (43) and dyslipidaemias (37) respectively.

Table 3: Efficacy parameters at baseline and follow-up visits in patients with Type 2 DM

		Mean (SD)	*P value (Paired T test)*
FBS (mg/dl)	Baseline	192.55 (67.65)	-
	Week 4	157.16 (44.53)	<0.0001
	Week 8	128.9 (25.64)	<0.0001
	Week 12	112.49 (17.77)	<0.0001
PPBS (mg/dl)	Baseline	268.63 (94.32)	-
	Week 4	224.28 (78.57)	<0.0001
	Week 8	194.71 (59.55)	<0.0001
	Week 12	169.86 (44.84)	<0.0001
HbA1C	Baseline	8.91 (1.63)	-

(%)	Week 12	6.88 (0.97)	<0.0001

As shown in table 3, statistically significant change is seen in all the efficacy parameters of glycemic control amongst diabetes mellitus patients. FBS- 112.49 (17.77), PPBS - 169.86 (44.84) and HbA1c - 6.88 (0.97) at 12 weeks. The *P value (Paired T test) was* <0.0001. Observed difference was statistically significant at each visit.



As shown in fig2, all the efficacy parameters for lipid profile that is- LDL, HDL, Total cholesterol and triglyceride levels showed statistically significant fall from baseline to 4th ,8th and 12th week. (Paired T test p>0.0001).

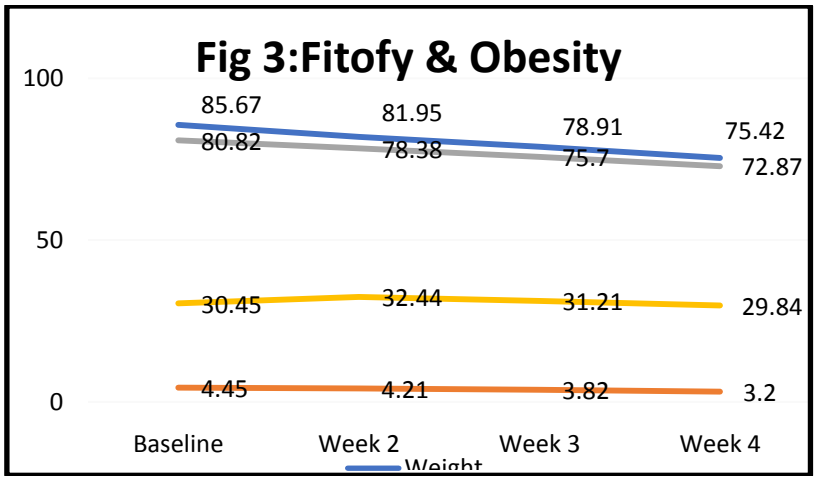


Fig 3 shows that all the efficacy parameters for obesity observed in the study including weight, hunger level and waist circumference showed highly statistically significant fall from baseline to 4th, 8th and 12th week. (Paired T test p>0.0001). In BMI, a statistically significant difference was observed between baseline and 2nd week. Reduction in calorie intake from baseline to 1, 2, 3 and 4 weeks was highly statistically significant (p < 0.0001).

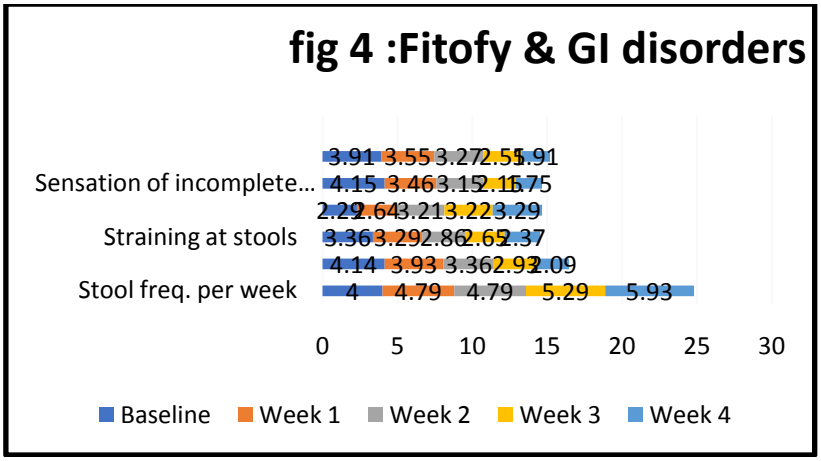


Fig 4 shows changes in various efficacy parameters for GI disorders over 4 wks. Significant reduction was observed in stool hardness and sensation of incomplete evacuation parameters (p- 0.02). Spontaneous defecation and bowel frequency per week showed good improvement.

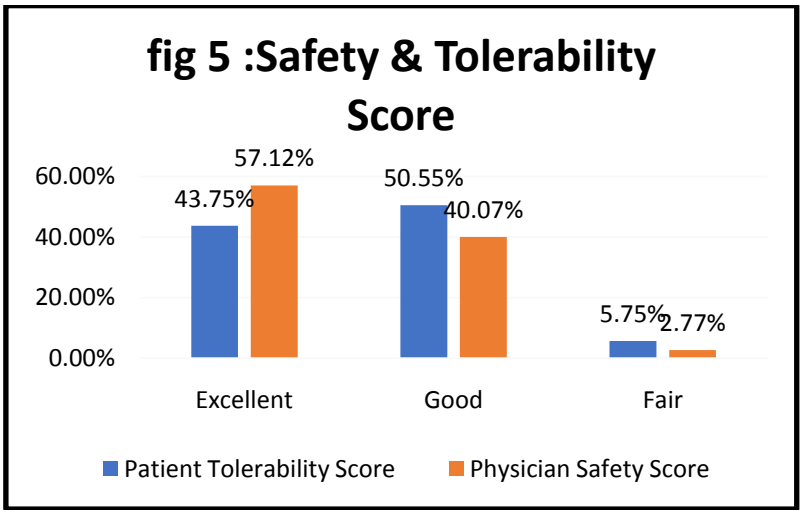


Figure 5 shows physicians' opinions on safety and patients' opinions on tolerability of DFSC. As per the healthcare professionals, good to excellent safety was observed in 97.19 % of the patient. No adverse event was reported by physician in any of the patients, A view of good to excellent tolerability with DFSC was opined by 84.30 % patients.

DISCUSSION

This is a prospective observational study (post marketing) conducted to assess the efficacy and safety of Fitofy, which is a nutraceutical blend of three dietary soluble fibers in various chronic metabolic disorders such as diabetes mellitus, dislipidemia, overweight and obesity and chronic GI disorders such as chronic constipation and irritable bowel syndrome (IBS).

In the present study statistically significant change is seen in all the efficacy parameters of glycemic control amongst type 2 diabetes mellitus patients such as fasting blood sugar (FBS), 2 h postprandial blood sugar (PPBS) and glycosylated hemoglobin (HbA1c) at 12 weeks after supplementation of DFSC (Fitofy). We have observed reduction of glycosylated hemoglobin (HbA1c, MD -2.03 %, P < 0.00001), fasting plasma glucose (FPG, MD -80.06 mgm/dl < 0.00001) and 2-h postprandial plasma glucose (MD -98.78 mgm/dl; P < 0.00001).

This is in line with the study conducted by Yajuan Xie et al [9]. and they have seen statistically significant effect of supplemental soluble dietary fiber on reduction of glycosylated hemoglobin (HbA1c, MD -0.63%, P < 0.00001), fasting plasma glucose (FPG, MD -0.89 mmol/LP < 0.00001) and 2-h postprandial plasma glucose (SMD -0.74; P < 0.00001) compared with control diets in patients with type 2 diabetes.

In patients with dyslipidemia, we have observed statistically significant reduction of LDL (LDL, MD -55.78 mgm/dl, P < 0.00001), Total cholesterol (TG, MD -75.78 mgm/dl < 0.00001)and Triglycerides (MD -80.78 mgm/dl; P < 0.00001). Our results are in line with Abed Ghavami et al [10]. Who conducted a recent systematic review for soluble

fiber supplementation and serum lipid profile. There was a significant reduction in LDL cholesterol (MD: −8.28 mg/dL −5.18), total cholesterol (TC) (MD: −10.82 mg/dL) and TGs (MD: −5.55 mg/dL, 95% CI: −10.31, −0.79) after soluble fiber supplementation. Each 5 g/d increase in soluble fiber supplementation had a significant reduction in TC and LDL cholesterol levels. This large meta-analysis of RCTs suggests that soluble fiber supplementation could contribute to the management of dyslipidemia and reduction of cardiovascular disease risk.

In overweight and obese patients, we have observed statistically significant reduction (p- <0.0001) in various efficacy parameters such as body weight (MD - 10.25 kg), waist circumference (MD - 7.95 cm), visceral fat (MD - 3.58 cm2), hunger level (MD - 1.24) and calorie intake (MD- 207.89 Kcal) over 4 weeks supplementation of DSFC (Fitofy). We have also noted a reduction in BMI (-1.99 Kg/m2) in the 2nd week. The results of our multicentric study with large sample size match with the previous study by Ami Shah et al [11]. to assess the efficacy and safety of Fitofy in overweight and obese patients. The study has shown statistically significant reduction in mean body weight (MD - 07.82 kg) and BMI (MD - 03.27 kg/M2).

In our study of patients with chronic GI disorders, statistically significant reduction was seen in various efficacy parameters such as stool hardness, sensation of incomplete evacuation over 4 weeks. We have also observed a good improvement in stool frequency per week and spontaneous defecation. These observed changes are in line with a meta-analysis conducted by Jing Yang et al. [12]. In which dietary fiber showed significant improvement over placebo in stool frequency (OR = 1.19; P < 0.05) and concluded that dietary fiber intake can obviously increase stool frequency in patients with constipation. Another randomized clinical trial conducted by Askin Erdogan et al. [13]. studied the effect of soluble/insoluble fiber and psyllium for chronic constipation and observed that soluble/insoluble fiber is equally effective for improvement in constipation symptoms and quality of life as psyllium.

We have observed encouraging results in relation to the safety and tolerability profile of DFSC. As per the healthcare professionals, good to excellent safety was observed in almost 98% of the patients. No adverse event was reported by the physician in any of the patients. A view of good to excellent tolerability with DFSC was opined by most (around 85 %) patients.

Limitations of study: This was a prospective observational, uncontrolled study conducted on a relatively smaller sample size and for shorter duration. A randomized, controlled clinical trial in a greater number of subjects with control of all the confounding factors is warranted.

CONCLUSION

As per this prospective observational post marketing study, the dietary fiber supplement combination of inulin, partially hydrolyzed guar gum, and resistant maltodextrin (DFSC) with proper diet therapy/modification is found to be safe and effective in causing significant improvements in efficacy parameters of various chronic metabolic disorders like type 2 DM, dyslipidemia, overweight/obesity and chronic GI disorders.

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