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Effect and Mechanism of *Virechana Karma* (Therapeutic Purgation) Over Fructose-Induced Metabolic Syndrome: An Experimental Study

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Abstract

Background. *Panchakarma* (biopurification methods) is one of the modes of ayurveda to treat disorders of the body. *Virechana karma* (therapeutic purgation), one among the Panchakarma, is a purification process that is commonly used to treat metabolic disorders like obesity and diabetes mellitus. Hence this study was planned to provide evidence through animal experiments. *Methods*. Albino rats were subject to Virechana karma (therapeutic purgation) to evaluate the influence of therapy and its mechanism over fructose-induced metabolic syndrome. *Results*. Results show that Virechana is effective in the management of the metabolic syndrome with decrease in the fecal fat content, fasting blood glucose, serum triglyceride, and reduced fatty changes in liver, heart, and kidney in comparison with the positive control group. *Conclusion*. Experimental evaluation showed decrease in fatty acid in the storage like liver, kidney, heart, and muscle adipose tissue can indirectly increase the insulin sensitivity in insulin receptor present at skeletal muscles.

Keywords

insulin sensitivity, insulin resistance, ayurveda, Panchakarma, metabolic syndrome

Incidences of insulin resistance are on the rise due to increase in rates of obesity. Metabolic syndrome may overtake smoking as the leading factor contributing to heart disease. The processes involved in obesity and insulin resistance include diet, inflammation, dyslipidemia, and impaired liver metabolism. Managing the subjects at an early may not only prevent diabetes but also reduce all possible complications due to its effect on multiple systems. Increased prevalence rate of diabetes worldwide is the prime factor for this and therefore proper screening, education, and assessment of patients is extremely important in obesity control and management.[1] Pathogenesis of metabolic syndrome says that reactive oxygen species accumulate, which cannot be quenched by adjacent peroxisomes; these reactive oxygen species reach the endoplasmic reticulum, leading to a compensatory process termed the *unfolded protein response*, driving further insulin resistance and eventually insulin deficiency. No obvious drug target exists in this pathway. Thus, the only rational therapeutic approaches remain altering hepatic substrate availability (dietary modification), reducing hepatic substrate flux (high fiber), or increasing mitochondrial efficiency (exercise).[2]

Panchakarma (biopurification method) is one among the many modes of ayurveda to treat disorders of the body. These are 5 specially designed procedures of internal purification of the body. Such purification allows the biological system to return to hemostasis, to rejuvenate rapidly, and also facilitates the desired pharmacotherapeutic effects of medicine. The elimination of waste products is known as *shodhana* (purification). These are performed in 3 phases—preparatory phase, main procedure, and postoperative phase. *Virechana karma* (therapeutic purgation) is a mode of main therapy in Panchakarma. Though many clinical studies carried out in ayurvedic institutions throughout the country have proved the clinical efficacy of this procedure in metabolic disorders like obesity, diabetes mellitus, it has not received much attention with regard to its

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mechanism and modern investigations possibly due to the conceptual compatibility difficulties. In classic texts, it has been clearly mentioned that these procedures, especially Virechana, can act as a curative, preventive, and health-promoting measure. This may be brought about by subtle changes at the cellular level by modulating physiological, biochemical, and immunological activities at the molecular level. It can be assumed that if it is possible to establish and standardize these procedures in experimental animals, it would be possible to make attempts to elicit the effects occurring at the subcellular level and mechanism, which are difficult to be performed in clinical settings.

This justifies the use of Virechana therapy to assess its effect in experimental models. Thus, this study aimed to "evaluate the efficacy of Virechana karma in fructose-induced metabolic syndrome."

The aims and objectives were the following:

- To evaluate the effect of Virechana karma in rats with fructose-induced metabolic syndrome.
- Mechanism of Virechana karma over insulin resistance.

Materials and Methods

- Wistar strain albino rats of either sex were procured from the animal house attached to the SDM Centre for Research in Ayurveda and Allied Sciences, Udupi, Karnataka, India.
- The study was conducted after obtaining the permission of Institutional Animal Ethics Committee (IAEC/02/2014-15/HS-07).

Source of Drugs

- Udvartana churna prepared out raw drug Kultha, mudga, triphala, sarspa, methika and yava obtained from SDM Ayurveda Pharmacy, Udupi.
- Trikatu choorna obtained from SDM Ayurveda Pharmacy, Udupi
- Moorchita tila taila obtained from SDM Ayurveda Pharmacy, Udupi
- Triphala kwatha churna obtained from SDM Ayurveda Pharmacy, Udupi
- Root of *Operculina turpethum* Linn from SDM Ayurveda Pharmacy, Udupi
- Eranda taila from SDM Ayurveda Pharmacy, Udupi
- Fructose was obtained from Loba Chemie Private Ltd. Mumbai, India

Standardization of Investigational Drug

Physicochemical characterization, determination of total ash, acid insoluble ash, and water-soluble ash, loss on drying at 110°C, water soluble extractive, and alcohol-soluble extractive tests were done as per Ayurvedic Pharmacopoeia of India standards.[3] Disintegration time of the tablets was assessed as per Indian Pharmacopoeia.[4] High-performance thin layer chromatography studies were done at SDM Centre for Research in Ayurveda and Allied Sciences, Kuthpady, Udupi, as per standard procedure vide analysis report 288/13073007-11.

Inclusion Criteria

1. Healthy albino rats of either sex were considered.
2. Weight ~150 to 250 g.

Exclusion Criteria

1. Weight <150 g and >250 g.
2. Pregnant and diseased rats.
3. Rats that are under trial of other experiments.

Animal Grouping

The selected animals were assigned to the following groups randomly and each group comprised 8 animals.

Group 1: Normal rats on normal laboratory diet
Group 2: Control rats on fructose water
Group 3: Rats on fructose water and subjected to Virechana (*Operculina turpethum* Linn root bark powder)
Group 4: Rats on fructose diet and subjected to Virechana (Eranda taila)

Dose Fixation and Schedule

The dose of the formulation was calculated by extrapolating the human dose to rat dose on the basis of body surface area ratio (conversion factor 0.018 for rats) by referring to the table of Paget and Barnes (1969)[5]:

For rats: Humans dose × 0.018 = x g / 200g. Rat X **x** 5 – y g / kg. of rat

Fructose Model Dose Fixation

For fructose-induced metabolic syndrome, the dose of fructose was fixed on the basis of a pilot study. Groups 2 and 3 received fructose 15% water to induce metabolic syndrome in 6 weeks. The dose was 15 g/100 mL = 75 g (fructose)/500 mL (distilled water) prepared in 1000-mL beaker after weighing fructose on a high-precision balance. Group 4 received fructose 55% and diet normal food to induce metabolic syndrome in 2 weeks (30 g/d/cage

Deepana pachana with Trikatu choorna:
Human dosage: 9 g/d
Rat dosage: 810 mg/d
162 mg/200 mg converted as 3 g/15 mL = 200 mg/mL
Snehapana with Moorchita taila (Table 1)
Virechana karma was induced by administering

Group 3: *Operculina turpethum* Linn root bark powder along with Triphala Kashaya 0.5 g/10 mL of rat dosage
Group 4: Eranda taila was used to induce with 1 mL/100 g of rat dosage.

Table 1. Dosage of Snehapana.

	Day						
Dose	1	2	3	4	5	6	7
Human (mL)	25	50	75	100	125	175	290
Rat (mL/200 g)	0.45	0.90	1.35	1.80	2.25	3.15	3.50

Schedule

Rats in Groups 2 and 3 received fructose-enriched water for 6 weeks and those group 4 received fructose-enriched diet for 2 weeks to induce metabolic syndrome, which was characterized by hyperglycemia, hypertriglyceridemia, and insulin resistance. After induction of metabolic syndrome, group 2 was kept as control rats with metabolic syndrome.

Purva karma (preoperative)

- Deepana pachana with Trikatu choorna along with Sarvanga udvartana and Ushna jala snaana for Rukshana (basal metabolic rate increasing)
- Snehapana with Moorchita tila taila (for internal oleation).
- Sarvanga abhyanga with Moorchita taila and Ushna jala snaana

Pradhana karma (operative)

Group 3 rats with metabolic syndrome were subjected to Virechana karma with *Operculina turpethum* Linn root bark powder along with Triphala kashaya, whereas group 4 rats were subjected to Virechana karma with Eranda taila.

Paschat karma (postoperative)

After Virechana Samsarjana in the form of peya (post–virechana low-carbohydrate diet) was administered once.

After the completion of the course of treatment, blood samples were obtained from orbital plexuses under ether anesthesia. After collection of the blood, the animal was sacrificed to dissect and collect heart, liver, kidney, colon, jejunum, and spleen for histopathological examination. The following parameters were measured based on standard laboratory guidelines[6]: body weight, food and water consumption before and after therapy, serum glucose, and serum lipid profile.

Assessment Criteria

Assessment criteria were based on.

a. Suppression of levels of biochemical parameters
b. Effect on histological changes of heart, liver, kidney, colon, pancreas, jejunum, and spleen.

Table 2. Effect of Virechana Karma on Blood Glucose.

Group	Blood Glucose (mg/dL), Mean ± Standard Error of Mean	% Difference
Normal control	75.66 ± 6.80	–
Fructose control	135.71 ± 9.40**	79.36 ↑[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	125.5 ± 6.48	7.52 ↓[b]
Test 2: Fructose diet: Virechana (Eranda taila)	79 ± 4.56**	41.52 ↓[b]

[a]Considered highly significant compared with normal control.
[b]Considered highly significant compared with fructose control.
**$P < .01$.

Table 3. Effect of Virechana Karma on Total Cholesterol.

Group	Total Serum Cholesterol (mg/kg); Mean ± Standard Error of Mean	% Difference
Normal control	31.16 ± 6.008	—
Positive control	64.48 ± 3.65	106.93 ↑[a]
Test 1: Fructose Water: Virechana (*Operculina turpethum* Linn root bark powder)	96 ± 4.04	48.88 ↓[b]
Test 2: Fructose diet: Virechana (Eranda taila)	102.8 ± 6.69	59.42 ↑[b]

[a]Considered highly significant compared with normal control.
[b]Considered highly significant compared with fructose control.

Observations and Results

Observations

After 2 hours of administering Virechana yoga, the effect of Virechana (therapeutic purgation) in formless watery stools was observed for 2 to 4 times within 4 hours. The stool was not watery but semisolid. In the evening, peya (post-virechana low-carbohydrate diet) was given.

Results

Analysis of data was done using 1-way analysis of variance followed by Dunnet multiple comparison *t* test with post hoc test using Graphpad Instat software.

P value is <.001. Data related to the effect of Virechana karma on blood glucose are shown in Table 2. The data obtained show a statistically highly significant reduction of blood glucose in tests 1 and 2 groups in comparison with control group. In test 2 groups, the effect was found to be better than in test 1 group.

Data related to the effect of Virechana karma on total cholesterol are shown in Table 3. The data obtained show a statistically significant increase of total cholesterol in both Tests 1 and 2

Table 4. Effect of Virechana Karma on High-Density Lipoprotein (HDL) Cholesterol.

Group	HDL Cholesterol (mg/dL); Mean ± Standard Error of Mean	% Difference
Normal control	17.66 ± 1.054	—
Positive control	40.32 ± 2.848	128.31 ↑[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	40.5 ± 3.723	0.44 ↓[b]
Test 2: Fructose diet: Virechana (Eranda taila)	68.4 ± 8.846	69.64 ↑[b]

[a]Considered highly significant compared with normal control.
[b]Considered highly significant compared with fructose control.

Table 5. Effect of Virechana Karma on Low-Density Lipoprotein (LDL) Cholesterol.

Group	LDL Cholesterol (mg/dL); Mean ± Standard Error of Mean	% Difference
Normal control	11.66 ± 1.333	—
Positive control	9.72 ± 0.54	−16.63 ↓[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	20.25 ± 1.386	108.33 ↑[b]
Test 2: Fructose Diet: Virechana (ERANDATAILA)	17.6 ± 1.470	81.06 ↑[b]

[a]Considered highly significant compared with normal control.
[b]Considered highly significant compared with fructose control.

groups in comparison with control group. However, in test 1 group, the increase was found to be less than in test 2 group.

Data related to the effect of Virechana karma on high-density lipoprotein cholesterol level are presented in Table 4. The data obtained show a statistically significant increase of high-density lipoprotein in test 2 group in comparison with control group. However, in test 1 group, a slight decrease was found in comparison with control group.

Data related to the Effect of Virechana karma on low-density lipoprotein cholesterol are shown in Table 5. The data obtained show a statistically significant increase of low-density lipoprotein in both tests 1 and 2 groups in comparison with normal control group. However, in positive control group, the decrease found in comparison with normal control group was statistically nonsignificant.

Data related to the effect of Virechana karma on triglycerides level are shown in Table 6. The data obtained show a statistically significant increase of triglycerides in both tests 1 and 2 groups in comparison with normal control group. However, in positive control group, the decrease found in comparison with normal control group was statistically nonsignificant.

Table 6. Effect of Virechana Karma on Triglycerides.

Group	Triglycerides (mg/dl); Mean ± Standard Error of Mean	% Difference
Normal control	81 ± 20.038	—
Positive control	256.14 ± 5.016	216.22 ↑[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	236.75 ± 2.920	7.57 ↓[b]
Test 2: Fructose diet: Virechana (Eranda taila)	246 ± 12.48	3.95 ↓[b]

[a]Considered highly significant compared with normal control.
[b]Considered highly significant compared with fructose control.

Table 7. Effect of Virechana Karma on Serum Creatinine.

Group	Serum Creatinine (mg/10 mL); Mean ± Standard Error of Mean	% Difference
Normal control	0.61 ± 0.17	—
Positive control	0.61 ± 0.01	0
Test 1 Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	0.81 ± 0.03	−32.78 ↑[a]
Test 2: Fructose Diet: Virechana (Eranda taila)	0.82 ± 0.06	−34.42 ↑[a]

[a]Statistically significant increase compared with normal control.

Table 8. Effect of Virechana Karma on Fecal Fat Content.

Group	Fecal Fat Content (%); Mean ± Standard Error of Mean	% Difference
Normal control	3.05 ± 0.36	—
Positive control	5.77 ± 0.84	0 ↑[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	3.09 ± 0.29	46.44 ↓[b]
Test 2: Fructose Diet: Virechana (Eranda taila)	3.42 ± 0.28	40.72 ↓[b]

[a]Considered statistically significant compared with normal control.
[b]Considered statistically significant compared with fructose control.

Data related to the effect of Virechana karma on serum creatinine are presented in Table 7. *P* value is .1820 and considered nonsignificant. The data obtained show a statistically significant increase of serum creatinine in both tests 1 and 2 groups in comparison with normal control group. However, there were no change founds between normal and positive control groups.

Data related to the effect of Virechana karma on fecal fat content are shown in Table 8. The data obtained show a

Table 9. Effect of Virechana Karma on Body Weight Changes.

Group	Body Weight Changes; Mean ± Standard Error of Mean	% Difference
Normal control	6.93 ± 3.669	—
Positive control	84.61 ± 8.48	−91.80 ↑[a]
Test 1: Fructose water: Virechana (*Operculina turpethum* Linn root bark powder)	26.64 ± 6.05	68.51 ↓[b]
Test 2: Fructose diet: Virechana (Eranda taila)	8.03 ± 2.35	90.50 ↓[b]

[a]Considered statistically significant compared with normal control.
[b]Considered statistically significant compared with fructose control.

statistically significant decrease of fecal fat content in both tests 1 and 2 groups in comparison with positive control group.

Data related to the effect of Virechana karma on body weight are presented in Table 9. The data obtained show a statistically significant increase of body weight in both tests 1 and 2 groups in comparison with positive control group.

Histopathological Examination

Sections of liver, heart, kidney, spleen, jejunum, pancreas, and colon were scanned under microscope at different magnifications. The following is the inference drawn.

Liver. Histopathological changes in liver can be found as changes observed in fatty changes, cell infiltration/hemorrhagic patches/cell depletion. In group 1, liver section from 2 rats exhibited almost normal cytoarchitecture; mild to moderate fatty changes were observed in sections from 2 rats and hemorrhagic patches of moderate intensity was observed in section from 1 rat. Mild to moderate cell infiltration could be observed in sections from 2 rats. Multiple lesions were observed in 3 rats. In liver sections from group 2, comparatively higher degree of pathological changes were observed. Moderate to severe cell depletion was observed in almost all the sections. Intense focal cell infiltration was observed in sections from two rats. Fatty changes of mild to moderate nature was also observed. Multiple lesions in single animal was observed in 4 of 7 rats. In group 3, the changes were much milder. Multiple lesions were not observed, and fatty changes were mild to moderate and cell infiltration was mild in comparison with group 2 lesions.

Heart. Microscopic examination of heart sections from group 1 revealed normal cytoarchitecture in sections from 5 rats. In 1 rat, mild myocarditis features were observed. In group 2, features of myocarditis were observed in 3 of 7 rats and in group 3, features of myocarditis were observed in only 1 of 6 rats.

Kidney. The main changes observed were fatty changes in tubular epithelium. In group 1, mild fatty changes were observed in 3 of 5 rats in the tubular epithelium but for this the cytoarchitecture was normal. In group 2, mild fatty changes were observed in 1 rat; 4 exhibited mild to moderate fatty changes while in 1 rat almost normal cytoarchitecture was observed. In group 3, kidneys from 4 rats exhibited normal cytoarchitecture, mild changes were observed in 1 rat, and mild to moderate change in another rat.

Spleen. Major feature observed was increase in the proportion of white pulp in all the groups. The increase was marked in all 6 rats in groups 1 and 2. In group 3, moderate increase was observed in 2 rats while the remaining 3 exhibited marked increase.

Pancreas. No major pathological changes could be observed in the pancreas. Difference in the number and cellularity of the islet of Langerhans was observed. Histological examination revealed normal pancreatic cytoarchitecture in all the groups. However, further analysis of the size and cellularity of islets showed interesting data. The number, size, and cellularity were evaluated in 18 fields. In group 1, 2 small-sized, 13 medium-sized, and 10 large-sized islets were observed. The cellularity was low in 1, medium in 14, and high in 10 islets. The figures for group 2 sections was 11 small-sized, 12 medium-sized, and 1 large-sized islet. The cellularity was low in 5, medium in 15, and high in 1 islet. In group 3, there were 12 small-sized, 6 medium-sized, and 2 large-sized islets.

Colon. Changes observed were epithelial disruption, edema, and inflammation in the epithelial layer; shortening of the epithelial layer, necrosis was also observed.

In group 1, all colon sections exhibited normal cytoarchitecure. In group 2, in 1 rat shortening of epithelial layer was observed and in another rat mild to moderate cell infiltration was observed. The colon sections from the remaining 4 rats exhibited normal cytoarchitecture. In group 3, colon sections from 5 rats exhibited normal cytoarchitecture while in 1 rat moderate necrosis of the epithelial layer was observed.

Jejunum. Changes observed were epithelial disruption, edema, and inflammation in the epithelial layer; shortening of the epithelial layer, necrosis of epithelial layer was also observed. In group 1, all jejunal sections exhibited normal cytoarchitecure. In group 2, in 1 rat shortening of epithelial layer was observed along with moderate to severe necrosis and in another rat mild epithelial disruption was observed. The jejuna sections from the remaining 4 rats exhibited normal cytoarchitecture. In group 3, normal cytoarchitecture was observed in 3 rats. Epithelial necrosis of moderate extension was observed in 2 rats and in 1 rat cell infiltration of moderate extent was observed.

Discussion

The main objective of carrying out this study was to determine the influence of Virechana over insulin resistance. This was done in the light of the fact that clinically, Panchakarma

therapy is being used extensively for treating metabolic disorders, often with good results.

Since it is the first study of its kind, it was thought worthwhile to assess the test procedures for other important parameters related to metabolic disorder effects as enumerated below. The discussion can be initiated by enumerating the results obtained and their implications and probable mechanisms of action.

Assessment Parameters and Histopathology

Histological examination and biochemical parameters did not revealed any test procedure–induced significant alterations in the microscopic profile of organs and biochemical changes.

During the process of Snehapana, only taila (sesame oil) is administered, and there is acceleration of fat utilization for energy in the absence of carbohydrates. This absence of carbohydrate replenishment promotes mobilization of fatty acids from the adipose tissue. As the process of gluconeogenesis leads to breakdown of the muscle adipose tissue,[7] the data obtained show a statistically significant increase of serum creatinine in both test 1 (0.81 ± 0.03, mean $\pm$ standard error of mean) and test 2 (0.82 ± 0.06, mean $\pm$ standard error of mean) groups in comparison with normal control group. However, there were no change found between normal and positive control groups.

There was significant increase in lipids such as total cholesterol, low-density lipoprotein, and high-density lipoprotein, and histopathology of kidney reveals fatty changes in tubular epithelium. In heart, the changes observed were mild myocarditis and fatty changes. These changes are self-replicating as seen in clinical subjects soon after Virechana karma. However, from the above factors we understand that during the process of Snehapana, there is a negative energy balance as it stimulates starvation.

This increase in the level of total cholesterol, low-density lipoprotein, high-density lipoprotein, and serum creatinine is suggestive of 2 facts; that first, in the group where Virechana is induced by *Operculina turpethum* Linn root bark powder, it is due to the process of gluconeogenesis taking place thus dragging fat from storage of heart, kidney, and muscle adipose tissue. This happens because single vega was observed.

Second, in the group where Virechana is induced by Eranda taila (castor oil), this rise is due to the process of hemoconcentration because the weight loss was observed by 90%, which is just 10% in the clinical study[8] and fecal fat content observed checked by oil read was reduced by 34% after Virechana, which has caused acute stress further leading to huge loss in blood glucose and rise in the lipids.[9]

Gastrium when filled with food, inhibits signals to suppress the feeding center, and a small quantity of fat is enough to cause this. Fats on entering the gastrium release cholecystokinin, which inhibits further eating. It also causes stimulation of the ventromedial nuclei of the hypothalamus, thus creating complete satiety. Next, when the chyme-containing fat enters the duodenum, the activity of the pylorus pump is depressed and the pylorus sphincter is slightly closed. Thus, stomach emptying is slowed. Since there is a carbohydrate restriction in the diet, ketosis is induced. Hence the process of Snehapana medically induces ketosis. This can be explained as follows: In the process of Snehapana, the source of energy is changed to proteins to begin with and then to fat, thus inducing ketosis. After digestion, the excessive fat is lost in the form of steatorrhea.

For the purpose of Shodhana chikitsa, the secretory action of the mucous membrane is exploited. The oil contains macromolecules of fat and micromolecules of the medicine. During the ingestion, the micromolecules of medicine are absorbed.

After the process of Snehapana, Sarvanga abhyanga with svedana in form of avgaha is done. It has been proved that lymphatic massage aids in water loss, and thus ultimately weight loss. Whereas sveda, which causes hemoconcentration by the process of svedana, also helps in burning calories.

After hemoconcentration is achieved, virechana is done on the fourth day. During the process of shodhana, the body fluids are influenced for therapeutic purposes. Here the body fluids are removed either through the upper or lower route. The gastrointestinal tract is lined by mucous membrane, which has a dual nature of absorption and secretion. The absorption nature is exploited for Shamana chikitsa and the secretory nature is exploited in Shodhana chikitsa. During the process of Virechana, cellular fluid is drained into the interstitial fluid, which is drained into the vascular compartment; from here it is drained into the gastrointestinal tract for elimination. Thus, Virechana is targeted to create a biochemical alteration as it modulates the fluid compartments of the body. During the process of Virechana, body fluid is drained out, which has dissolved biochemicals in them.

Thus, Virechana has a 3-part mechanism in current study; the drugs increase the secretion by irritating the mucous membrane of the gastrointestinal tract. As seen in histopathological examination, there were changes in jejunal epithelial disruption, edema and inflammation in the epithelial layer, shortening of the epithelial layer, necrosis of epithelial layer. Similar features were present with colon histopathology with changes as epithelial disruption, edema and inflammation in the epithelial layer, shortening of the epithelial layer; necrosis was also observed in present study.

Second, it prevents absorption of nutrients and last, it increases the gastrointestinal motility. These characteristic features may be reason for the changes in histopathology of liver observed in the present study with decrease in fatty changes in test 2 group in comparison with positive control group, which is further signified with decrease in the body weight, serum triglyceride, fecal fat content as well as blood glucose levels with $P < .001$.

In the pathogenesis of insulin resistance, excessive fatty acid derivatives interfere with hepaticinsulin signal transduction. Reactive oxygen species accumulate, which cannot be quenched by adjacent peroxisomes; these reactive oxygen species reach the endoplasmic reticulum, leading to a compensatory process termed the *unfolded protein response*, driving further insulin resistance and eventually insulin deficiency.[10]

In a nutshell, therapy showed the decrease fatty acid in the storage like liver, kidney, heart, and adipose tissue can also indirectly increase the insulin sensitivity in insulin receptor present at skeletal muscles. In addition, size and number were decreased after the therapy in islets of Langerhans of pancreases shows decrease in resistance. Therefore, Virechana therapy showed its target-specific therapy for insulin resistance.

Probable Mode of Action

Virechana drugs carry out the therapeutic purgation due to their prabhava (potency). As these drugs are having Jala and Prithvi Mahabhuta dominancy, they have a natural tendency to go downward and thus they can help in induction of purgation. It has already been described that the waste products wherever present in the body, in extracellular, intracellular, or in plasma, can be brought into intestine to maintain the homogeneity from where it can be eliminated out of body by the action of intestine, which is induced by Virechana drug. Castor oil used in the Virechana karma gets hydrolyzed in small intestine by lipase to give ricinoleic acid, which irritates and requires bile for hydrolysis. Bile serves as a means for excretion of several important waste products from the body. These include bilirubin, an end-product of hemoglobin destruction and excesses of cholesterol synthesized by the liver cells.[11(pp117-119),12]

Further Scope of Study

- The reference *Charaka Sutra* chapter 17 verse 78-80 throws light on the issue of fat metabolism vis-a-vis insulin resistance. Further animal experimentation may be designed on it.[11]
- Actions over gastrointestinal tract: 2 important functions of the gastrointestinal tract, especially of small intestine, are secretion and absorption. Absorption occurs by 2 pathways—paracellular and transcellular. The individual epithelial cells are joined by a tight junction. Ions and water pass through these junctions during absorption and secretion. This pathway is known as paracellular pathway. This pathway is made up of small water-filled pores of channels. They remain closed during resting state and open and dilate during absorption. Furthermore, it has been shown that pumps and carrier proteins play important role in this activity. In the transcellular mechanism, Na^+ pump present in the basolateral membrane actively transports Na^+ out of the mucosal cells into the intracellular space.[13]
- Thus, the above mentioned mechanisms, that is, physical and physiological barriers, propulsion of the food, ion and water absorption mechanism, and presence of immune and inflammatory cells, form readily available substrates for the modulatory activity of the therapeutic measures like Virechana. It would be advisable to study the effect of Virechana on the above mechanism.

Conclusion

The result suggests that Virechana karma and preprocessing procedures both have good fat metabolism activity against experimental models representing fructose-induced metabolism syndrome over insulin resistance, body weight, and blood glucose level. The decreased fatty acid in the storage like liver, kidney, heart, and adipose tissue can also indirectly increase the insulin sensitivity in insulin receptor present at skeletal muscles. In addition, size was decreased after the therapy in islets of Langerhans of pancreases shows decrease in resistance. Thus, Virechana karma showed its target-specific therapy for insulin resistance. The study provides experimental evidence for the efficacy of Virechana in fructose-induced metabolic syndrome.

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Authors Contributions

AC contributed toward concepts, design, definition of intellectual content, literature search, experimental studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review, and agrees to act at guarantor. PNR contributed toward concepts, design, definition of intellectual content, experimental studies, data acquisition, statistical analysis, manuscript editing, and manuscript review. MAK contributed toward concepts, design, definition of intellectual content, literature search, experimental studies, data acquisition, statistical analysis, manuscript preparation, manuscript editing, manuscript review, and agrees to act at guarantor. BR contributed toward concepts, design, definition of intellectual content, literature search, experimental studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, manuscript review, and agrees to act at guarantor. NR contributed toward concepts, design, definition of intellectual content, literature search, experimental studies, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript editing, and manuscript review. MR contributed toward concepts, design, definition of intellectual content, literature search, experimental studies, data acquisition, data analysis, and manuscript review.

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Ethical Approval

The study was conducted after obtaining the permission of Institutional Animal Ethics Committee (IAEC/02/2014-15/HS-07).

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