**Review Article**

# Prevention of metabolic risks by *Kalabhojanam* strategy of Ayurveda

**Neha Pandey Prakash[1], Vishnu Bali Mishra[2], Bhaswati Bhattacharya[3], Arvind Kumar[4], Y.S. Raghuram[5], Bhadresh Naik[6], Mahesh Kumar Dadhich[7], P. Rammanohar[8], S. Gopakumar[9], Yamini Bhushan Tripathi[10], Satyendra Narayan Ojha[11], Girendra Singh Tomar[12], Jyoti Shanker Tripathi[13], Pawan Kumar Godatwar[14], Tanuja Nesari[15], Sanjeev Sharma[16], Shri Krishna Khandel[17], Madhaw Singh Baghel[18], Banwari Lal Gaur[19], Sanjeev Rastogi[20], Rajesh Kotecha[21], Deep Narayan Pandey[22]***

[1]Yajurvid Pharma; Yajurvid Ayurveda, Ratan Industrial Area, Jaipur 303904, Rajasthan, INDIA; [2]Ayurvedpuram, Prayagraj 211001, Uttar Pradesh INDIA; [3]Weill Cornell Medical College, New York, USA; [4] Regional Ayurveda Research Institute (Central Council for Research in Ayurvedic Sciences), Itanagar 791111, Arunachal Pradesh INDIA; [5] Department of Kaya Chikitsa, A.L.N. Rao Memorial Ayurvedic Medical College, Koppa, Karnataka INDIA; [6]Nilkanth Nuerospine Clinic, Khara Abrama, Navsari, Gujarat INDIA;[7] Department of Dravyaguna, MSM Institute of Ayurveda, BPS Women University, Khanpur Kalan, Sonipat 131305, Haryana INDIA; [8] Amrita VishwaVidyapeetham, Amrita School of Ayurveda, Amritapuri, Kollam 690525 Kerala INDIA;[9] Government Ayurveda College, Thiruvananthapuram 695001, Kerala INDIA;[10] Faculty of Ayurveda, Department of Medicinal Chemistry, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, Uttar Pradesh, INDIA; [11] Hon. Annasaheb Dange Ayurveda Medical College, Ashta, Sangli 416301, Maharashtra, INDIA;[12] Formerly at Department of Kaya Chikitsa, Government Ayurvedic College, Handia, Allahabad, Uttar Pradesh INDIA; [13]Department of Kayachikitsa, Faculty of Ayurveda, Institute of Medical Sciences, Banaras Hindu University, Varanasi 221005, Uttar Pradesh INDIA; [14] Department of Roga Nidana, National Institute of Ayurveda, , Jaipur 302002, Rajasthan INDIA; [15] All India Institute of Ayurveda, Gautampuri, SaritaVihar, New Delhi 110076, INDIA; [16] National Institute of Ayurveda, Jaipur 302002, Rajasthan INDIA; [17]Arogya Laxmi Ayurvedic Healthcare, Jaipur 302017, Rajasthan INDIA; Formerly at National Institute of Ayurveda, Jaipur 302002, Rajasthan INDIA; [18]Arogya Laxmi Ayurvedic Healthcare, Jaipur 302017, Rajasthan INDIA; Formerly at Ayurveda Chair, University of Debrecen, HUNGARY; Formerly at IPGT&RA, Gujarat Ayurved University, Jamnagar 361 008, Gujarat INDIA; [19]Formerly at Dr. Sarvepalli Radhakrishnan Rajasthan Ayurved University, Jodhpur 342037, Rajasthan INDIA; [20] Department of Kaya Chikitsa, State Ayurvedic College and Hospital, Lucknow, 226003, India; [21] Government of India, Ministry of AYUSH, New Delhi, INDIA; [22*] Department of Environment/Forests, Government of Rajasthan, Secretariat, Jaipur 302005, Rajasthan INDIA

*Corresponding Author's email: dnpandey@gmail.com

Date of 1st submission : 19 May 2019 | Date of Re-submission:30 May 2020 | Date of Acceptance: 15 June 2020

**ABSTRACT**

Metabolic risks are a global challenge. These risks are although modifiable by lifestyle, and physical activity to some extent, they are primarily related to dietary consumption. Considering a clear relationship of diet and metabolic risk factors, we hypothesised that an evidence-based, and widely applicable solution may be found in Ayurvedic dietetics. From among a large number of dietary strategies noted in Ayurveda classics, *kalabhojanam*—intake of food at a scheduled time, and not *ad libitum*—is suggested to be the best strategy to confer good health. Accordingly, using a novel methodology to provide fresh interpretation of known facts from *Samhitas*, scientific research on time-restricted feeding (TRF) and experiential knowledge, here we present the results of synthesis as usable knowledge for mass application. Results of this

synthesis demonstrate the indispensable value of *kalabhojanam* for maintaining the metabolic health. In translating these findings for better health among the masses, care must be taken that while *kalabhojanam* has definite elements of scheduled feeding, but it is much more comprehensive than time-restricted feeding. Accordingly, it should be adopted in a comprehensive manner according to Ayurvedic insights presented in this analysis. This study brings out that because irregular eating patterns are detrimental to metabolic health, *Kalabhojanam* being a robust non-pharmaceutical strategy may be helpful in prevention of metabolic diseases.

**Keywords:** Ayurveda; Healthspan, Kalabhojanam; Metabolic syndrome;Time-Restricted Feeding

**Annals Ayurvedic Med. 2020; 9 (2) 116-129**

## Introduction

Metabolic risks are predominantly associated with cardiovascular disease and diabetes, and together were responsible for 15·9% and 8·9% of the disability adjusted life years (DALYs) in India in 2016. This is up from 7·0% and 4·5% of the DALYs in 1990.[1]In India and elsewhere, these risks include high systolic blood pressure, high fasting plasma glucose, high total cholesterol, high body-mass index, impaired kidney function and low bone mineral density. Metabolic risks, although modifiable by physical activity and lifestyles, are primarily related to dietary consumption.[2,3]Accordingly, here we argue that a meaningful answer to address the challenge is likely to be found in dietary strategies of Ayurveda. *Charaka Samhita* of 200 BC—which is a redaction of *Agnivesha Tantra* that is believed to have been coded as far back as 900 BC—suggests that amidst all the dietary strategies that confer good health, ***kalabhojanam***, i.e., intake of food at a scheduled time, and not *ad libitum*, is the best strategy.[4] The literal meaning of ***kalabhojanam*** is meal timing or *kala* (time) of meal (*bhojanam*).This strategy, if stands the scrutiny of contemporary science, holds a great translational promise against metabolic diseases. Thus, in the light of available research across disciplines, regardless of whether or not it takes inspiration from Ayurveda, we explore the potential of *kalabhojanam* as a non-pharmaceutical intervention in prevention of metabolic diseases.

In writing this analysis, we have followed a method involving co-production and co-synthesis to produce usable knowledge.[5,6] We have drawn on three distinct sources of knowledge: Samhita classics, contemporary scientific research and experiential knowledge of *Ayurveda* practitioners. To begin with, with the help of PubMed, Scopus, Web of Science, and Google Scholar a comprehensive database of published research was assembled on fasting strategies including caloric restriction, time-restricted feeding, intermittent fasting, periodic fasting, fasting-mimicking diet, meal frequency and meal timing. Form this pool of 20,400 papers, 228 papers on time-restricted feeding (TRF) and related interventions were identified for primary screening for this review. Based on a careful reading of these papers, a representative sample was identified and cited here to develop a scientific understanding on the subject. In addition, in order to draw on an extensive pool of experiential knowledge, a diverse team of authors was assembled, representing: (i) multiple geographies of work areas, (ii) institutional diversity, (iii) variety of disciplines and domains of knowledge within Ayurveda, (iv) varying length of clinical experience, teaching or research, and, (v) experience of work in policy, planning and governance. In addition, the draft manuscript was subjected to open peer review (OPR) among a group of 219 Vaidyas, of which 32 responded, working across many countries. OPR is a cornerstone of the emergent Open Science agenda and serves important purpose of good science.[7,8] Accordingly, an integrated stock of insights are presented in this analysis. Collaborative approach applied here is useful for production of accurate and usable knowledge for healthcare.

In contemporary scientific studies, a closely related strategy known as time-restricted feeding, a form of intermittent fasting with reduced meal frequency has attracted serious attention of researchers. TRF limits daily intake of food to a 4 to 12 hour time slot during 24-hours. It is a daily restraint imposed on the food intake timing without any reduction in caloric intake.[9-11]Although scientific interest

in scheduled feeding is recent, restriction on the time of eating to promote health span is an ancient strategy of Ayurveda.

As we intend to draw scientific support for *kalabhojanam* from the research on contemporary TRF strategy, a brief clarification on contrary views is necessary. First, acontrary point of view is that *kalabhojanam* has less to do with a fixed time interval between two meals. It is rather more related to the time of feeling hungry, after the previous meal has been digested, that determines the gap between two meals. *Kala* in Ayurveda refers to 'appropriate time' and not merely time. Thus, it is always determined in synchronisation with individual physiology. Second, it can further be argued that there can be variations in this window of meal timing on the basis of dynamic nature of *agni* and thus the state of digestive system of each individual each day.

It is also pertinent to note here that *kalabhojanam* does not mean that food can be taken at will during the 24 hours. It must conform to and be in coherence with *dinacharya* such as waking-up and remaining awake during the day and sleep timings during night.[12] Further, while consuming food just once a day is the best strategy[4] and will automatically have a longer fasting period, but a second meal is neither prohibited nor is likely to impair *agni* or sleep.[13] Yet, even if the food is consumed twice during a day by those whose digestive system is in optimal state[14], the feeding time must remain restricted during morning to evening (i.e., a maximum of 12-hour eating window and thus a minimum 12-hour gap), and not during the night.[15] Thus, it extends the window between evening meal and morning meal. As *dinacharya* involves waking, elimination, hygiene, physical activity, application of oil, and many more, a person cannot eat soon after waking up in the morning. The time of first meal, therefore, is often after about 2 to 3 hours from waking up, except perhaps for those who prefer a very early eating. Thus, feeding time further gets restricted during 8.00 ante meridiem (am) to 5.00 post meridiem (pm) or so depending upon when one feels hungry during this available window of eating opportunity.

There is another important difference between *kalabhojanam* and TRF that practitioners need to keep in mind. Ayurveda suggests that even if what one has consumed in the morning is not properly digested, a second meal in the evening may not be harmful. But if the evening meal has not been digested, then eating during the morning next day may lead to undesirable consequences due to indigestion.[16] A morning meal does not lead to indigestion even when *agni* is weak. However, evening meal must always be light.[15]

It is also worth clarifying that meal-time alone is not the solitary factor that has relevance for diet, yet it is of prime significance. Ayurveda has a very comprehensive diet-science.[17] Indeed, there are a large number of references on food, diet and dietetics, embedded in different contexts in Ayurveda (Table 1). For example, one of the most fundamental guidance suggests that since many troublesome diseases are caused by irregular dieting, the wise should eat wholesome, measured and timely food with self-restraint.[18] Also, diet is not the only factor relevant in metabolic risks. Many other factors including physical inactivity, sedentary lifestyles and unhealthy diet are important.[19, 20] In this article, however, the focus is on meal-timings as described by *kalabhojanam* because among all the factors that confer good health, it is of prime significance. *Kalabhojanam* is described in the context of *agryasangraha*, i.e., interventions and materials that are of principal significance for achieving a particular objective.This clearly implies that assuming that one follows every guidance of Ayurveda to achieve good health, but compromises or ignores just the *kalabhojanam*,sustainable health span may remain unachievable. *Kalabhojanam*, therefore, is an indispensable component to confer *arogya*. Finally, treating metabolic challenges is a global priority that should not rely merely on a medicalized approach.[21] It is of paramount importance to draw on widely applicable, acceptable and easily implementable non-pharmaceutical interventions to solve contemporary health challenges.[22]

Knowledge is emerging that metabolism is a function of many factors other than calories that alter our nutrition, especially when and how we eat. The relationship of circadian rhythms, time-restricted feeding and healthspan

emphasizes mental choices on how we construct our day, awareness of food processing times inside the body, and the impact of our lifestyle choices on longevity. The tenets of *kalabhojanam* correlate with new data validating TRF using animal models and clinical studies in humans and offer a novel opportunity to use the large repository of non-pharmacological interventions to solve the contemporary health challenges associated with metabolic diseases.

**Table 1: Interpretation and translational significance of *Kalabhojanam* and TRF**

| No. | *Kalabhojanam* | TRF | Interpretation |
|---|---|---|---|
| 1. | The appropriate *kala* (time) for a meal is after the evacuation of bowels and urine; when the heart/mind has become free from malice; *Doshas* have moved towards equilibrium; belching is clear; flatus moves out naturally, digestive fire is kindled and person is hungry; and his/her body feels light[23]. | TRF refers to the strategy of intake of food at a scheduled time or during a window-of-time, and not *ad libitum*.TRF is a form of intermittent fasting that may also have the elements of reduced meal frequency. | Taking food *ad libitum* is not permitted both in *kalabhojanam* as well as TRF. Both strategies refer to scheduled feeding and reduction in meal frequency, but TRF spans through a window-of-time when eating is permitted, and *Kalabhojanam* is not merely related to 'time', but has more comprehensive and inclusive meaning as noted in column related to *kalabhojanam* in this table. |
| 2. | According to Ayurveda, time of food intake depends on several factors including, but not limited to, difference in individual physical constitutions, type and nature of food, emotional status of person, status of *agni*, status of digestion of previous diet, functioning of excretory system, seasonal and climatic variations, individual energy requirements and so on[24]. However, for a healthy person it is certain that one should not consume more than two meals in a day[14] and temporal-spacing among these two meals should be decided by specific factors[23]. | TRF concentrates more on time and less on other factors. Unlike Ayurveda, TRF does not limit the number of time one can take food, but limits the temporal duration within which one can eat or fast. | Prohibition of *ad libitum* eating in TRF is clearly incorporated in *kalabhojanam* as well, but Ayurvedic strategy is much more comprehensive. Indeed, coupled with sedentary life and suppression of non-suppressible urges, non-adherence to *kalabhojanam* is the key factor that leads to perpetual illnesses.[25] |
| 3. | Among the multitude of factors[26,27], at a minimum Ayurveda recommends to practice being *hitashi* (consumption of wholesome diet), *mitashi* (consumption in measured quantity), and *kalabhoji* (consumption at appropriate time)[18].Here, caloric restriction has also received equal emphasis in Ayurveda, but as *kalabhojanam* has been placed in *agryasangraha*, it carries the fundamental significance among all these factors. | Research in TRF has moved in both directions: TRF without caloric restriction and TRF with caloric restriction. Yet, the benefits are realized even without caloric restriction, perhaps because time-window may act as inherent restriction on the quantity of food one would often consume.Thus, time of eating has prime significance in TRF as well. | Even as 'time of taking food' has some differences in terms of comprehensiveness of the meaning in Ayurveda and TRF, yet in both streams of knowledge it has prime and overriding significance. The translational value[28,29] of this understanding is that even if one follows every guidance of Ayurveda to achieve good health, but ignores the *kalabhojanam*, sustainable healthspan may not be achievable. However, while implementing this strategy, *kala* should be interpreted in a comprehensive way as proposed by Ayurveda (see, ref.[23] ). |
| 4. | Two precondition for adherence to *kalabhojanam* are being *jitendriya* (person who has control over sense organs; self-restraint) and awareness of the consequences of diseases that develop due to irregular dieting[18].Without a firm resolve to comply, *hitashanam*, *mitashanam* or *kalabhojanam* does not work. | Enablers of TRF include deciding and adhering to a routine, family support, personal commitment, adjustment in work schedule, and resisting the temptation during social events and festivities. | At a personal level, self-restraint and awareness of the consequences of diseases are important enablers of *kalabhojanam* and TRF. At the family and community level, external support and facilitation also matters. In cases involving clustered metabolic risks, multimodal interventions such as diet and physical activity may have more beneficial effects.[30] |

**Significance of *kalabhojanam* and TRF**

Our interest in *kalabhojanam* is driven by four important reasons:

One, this strategy is mentioned in the context of *agryasangraha* (i.e., collections of best food articles, factors, drugs and actions for various conditions). Thus, *kalabhojanam* is not an ordinary strategy. It is an extraordinary and leading principle that confers *arogya* (i.e., disease-free lifespan or healthspan). Accordingly, it has remarkable ramifications for public health worldwide.

Two, a large number of animal studies as well as a few human clinical trials on time-restricted feeding provide hope that it can be a leading strategy to prevent metabolic diseases and age-related pathogenesis plaguing India.

Three, while *Charaka Samhita* pronounced the principle of *kalabhojanam* along with guidance on its application, contemporary studies have provided more nuanced evidence about the vital importance of restricting the habit of eating *ad libitum*. In addition, contemporary studies also elucidate the mechanism of action through which *kalabhojanam* prevents metabolic diseases.[9,31]

Finally, it must be emphasised that a large body of research on preventive and therapeutic strategies is being published globally that may be useful to comprehend Ayurvedic principles, and even though these works do not cite Ayurveda, it is nevertheless possible to examine coherence or incoherence in contemporary science and Ayurvedic Samhitas.[22,32] Generating evidence through fresh interpretation of available science is of vital importance.[33] This paper is an illustration of that potential.

**Circadian rhythms, time-restricted feeding and healthspan**

Circadian rhythms are daily 24- hour rhythms in metabolism, physiology, and behaviour that are sustained under constant daylight or darkness during night. The discovery of the molecular mechanisms underlying the circadian clock, which functions in practically every cell in human body to coordinate biological processes, to anticipate and adapt to daily rhythmic changes in the environment, is considered as one of the major biomedical breakthroughs in the 20th century.[34] The role of circadian clock in a wide range of biological functions,health and diseases is now well understood. Among these, interactions between the clock and energy metabolism is a leading field of research. Research has also now established the role of circadian rhythms in sleep and health,[35] mental health,[36] neurodegenerative diseases,[37] and cognitive impairment.[38] Disruptions of the circadian clock can result into metabolic dysfunctions that result in obesity, diabetes, and several other metabolic disorders.[34]

Studies in both humans and animal models have linked circadian disruptions, either genetic (e.g., mutations in clock genes) or environmental (e.g., frequent circadian phase shifts), to a range of diseases, including cardiovascular disease, inflammatory bowel disease, immune-related disorders (e.g., rheumatoid arthritis and asthma), various cancers, neurodegenerative disorders, cognitive impairment, psychiatric illness, and many others.[34,39] Studies on animals and humans suggest that eating restrictions for as little as 16 hours can improve health indicators and prevent or break the chain of pathogenesis. The mechanisms of action involve a metabolic shift to fat metabolism, ketone production, and stimulation of adaptive cellular stress responses that prevent and repair molecular damage.[40]

Unlike *kalabhojanam*, no specific attention is given to nutrient quality or quantity in TRF. However,both *kalabhojanam* and TRF are aligned to circadian rhythms because the circadian clock intimately interacts with nutrient-sensing pathways. Due to *ad libitum* or frequent irregular eating there is no scheduled fasting period.This results in elevated levels of fed-state physiology and disturbs the normal counter-regulatory metabolic state that occurs during fasting.[41] Chronic circadian rhythm disruptions, driven by *ad libitum* feeding, amplify the risk of metabolic diseases. On the contrary, daily cycles of feeding and fasting even without caloric reduction, sustain

robust diurnal rhythms and can alleviate metabolic diseases.[42] Synergistic interactions between the circadian oscillator and feeding-fasting signals ensure that anabolic and catabolic types of metabolism are regulated in a coordinated manner, in synchrony with the activity-rest cycle.[41]

In TRF as well as *kalabhojanam*, strategy of timing of food consumption independent of total caloric intake and macronutrient quality has emerged as a critical factor in maintaining metabolic health.[43] For instance, when healthy adults eat identical meals at breakfast, lunch or dinner, the postprandial glucose rise is lowest after breakfast and highest after dinner,[44] as if the dinner were twice the size of the breakfast. In addition, when healthy adults are given a constant glucose infusion over 24 hours, glycemia rises at night and falls around dawn. These data indicate that when a meal is eaten determines the physiologic response to nutrient availability as much as what and how much is eaten.[42]

Caloric restriction (CR) is feeding strategy consisting of chronic reduction of total calorie intake without malnutrition. Together with intermittent fasting—which can be considered as a particular form of CR in which episodes of *ad libitum* feeding are alternated with episodes of up to zero caloric uptake, CR confers improvement in healthspan.[45] In Ayurveda, a similar but not exactly same, strategy is known as *mitashanam* (see Table 1 for details).Together with TRF, *kalabhojanam* or intermittent fasting, CR has been the leading non-pharmaceutical intervention to improve human healthspan.[45] Yet the research is now discovering easier and more acceptable ways such as TRF that provide similar health benefits.

This emerging area of research about the independent consequences of variations in meal frequency, by controlling the time of feeding and fasting, on the incidence or amelioration of multiple age-related diseases, including cardiovascular disease, diabetes, cancer, and dementia has now become an important pursuit of science.[11,41,46,47] While caloric restriction is an important strategy,[45,48] recent studies are starting to reveal that healthspan extension can be achieved by interventions that do not require an overall reduction in caloric intake.[9]

**Animal Studies**

In many experimental animal studies, the reduction in energy intake encourages the animals to consume their entire quota of daily food in a very short interval, thus promoting a longer fasting period than when consuming standard or calorie-rich diets.[49] Although nocturnal rodents with access to food eat mainly at night, they also feed during the day. This behaviour is found to correlate with gains in body weight.[49] Clearly then, these observations raise the question of whether the timing of food consumption (i.e, either feeding duration or circadian timing) is a determinant of metabolic health, independent of total caloric intake and quality of diet.[9] Indeed, it is possible that initiating the fasting response every day or at specific times is in itself advantageous to health. For, this potentially clarifies why dietary-dilution, a type of CR in which mice eat throughout day to compensate for the low density of energy in their food, does not result in extended life-span.[50] Thus, chronic CR may improve health, at least to some extent, through an extended period of fasting. In addition to appropriate caloric intake, a healthy diet should have a diversity of plant-based foods, low amounts of animal source foods, unsaturated rather than saturated fats, low amount of salt, and, if one cannot avoid altogether then small amounts of refined grains, highly processed foods, and added sugars[20].

Although data on the long-term effects of TRF on longevity are not yet available, studies in rodents have shown that TRF can confer protection against several detrimental metabolic consequences of a contemporary diet (that is high in fat and high in carbohydrates and refined sugars), through reduction in body weight, increase in energy expenditure, improved glycemic control and lower insulin levels, decrease in hepatic fat and hyperlipidemia, and attenuated inflammatory outcomes, even when food intake or body weight or both are matched to the control group.[51-54] For instance, time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed on

a high-fat diet. In an experiment,[51] mice undergoing TRF consumed equivalent calories from high-fat diet were found protected against obesity, hyperinsulinemia, hepatic steatosis, and inflammation and had improved motor coordination. The TRF strategy improved CREB (CREB is a critical neuronal transcription factor that regulates normal physiological function), mTOR (mTOR is a serine or threonine protein kinase that regulates cell growth, cell proliferation, cell motility, cell survival, protein synthesis, and transcription), and AMPK pathway function and oscillations of the circadian clock and their target gene expression. These changes in catabolic and anabolic pathways altered liver metabolome and improved nutrient utilization and energy expenditure. Thus, TRF turns out to be a non-pharmaceutical strategy against obesity and associated diseases.[51,55] These findings clearly lend support to *kalabhojanam* for inclusion in *agryasangraha* as an extraordinary and indispensable strategy for achieving *arogya*.

The molecular mechanisms responsible for the effects of altered meal patterns on metabolic health seem to be related, partly, to the synchronization between the time of fasting-feeding and the circadian rhythm.[42,56] TRF can also protect clock mutant mice from obesity without changes in activity or calories.[56] The circadian clock provides a conserved mechanism that allows organisms to anticipate and respond to environmental changes. This perpetual rhythm leads to the timely expression of clock-controlled genes, especially those encompassing enzymes and regulatory molecules that mediate physiological and metabolic functions.[9] There is evidence for a strong relation between the circadian clock and metabolism, as both share some common regulators. Indeed, TRF can restore cycling of metabolic regulators, such as nicotinamide-phosphoribosyl transferase (NAMPT), cAMP response element–binding protein, mTOR, AMPK, or the insulin signalling pathway, all of which are relevant to conferring lifespan and healthspan benefits of CR.[51] Recent studies have further substantiated earlier findings that TRF improves health and survival in male mice independent of diet composition and calories.[43] Indeed TRF can attenuate the adverse metabolic consequences, such as diet-induced pathogenesis, of high-fat, high-sucrose, or high-fructose diets in rodents and insects.[42,57]

**Human Clinical Studies**

How does TRF perform in humans? Here are some studies that provide useful insights.

Effects of mealtime in 420 subjects participating in a 20-week weight-loss treatment programme found that subjects who ate their daily main meal at earlier times of the day showed a more rapid loss of body weight.[58] Indeed, similar to what has been observed in animal models, early eaters and late eaters showed similar energy intake, dietary composition, and estimated energy expenditure,[58] suggesting a better metabolic balance in early eaters.[34] Comprehensive reviews have also concluded that TRF regimens achieved a superior effect in promoting weight-loss and reducing fasting glucose compared to unrestricted time in meal consumption.[59]

All results from TRF trials in human subjects also appear to depend on the distribution of meals during the day and the duration of fasting.[10,47,60-62] Limiting food intake to the middle of the day decreased body weight or body fat, fasting glucose and insulin levels, insulin resistance, hyperlipidemia, and inflammation and produced mild caloric restriction and weight loss, without calorie counting.[61,63,64] Likewise, metabolic markers improved in a group of people eating an isocaloric diet with a bigger breakfast and a smaller dinner,[64,65] and type 2 diabetic patients under hypocaloric diet obtained better metabolic outcome by eating most of their daily allotment in the first half of the day rather than divided into six meals throughout the day.[66] On the contrary, restricting food intake to the late afternoon or evening either produced mostly no results or worsened glucose levels, β cell responsiveness, blood pressure, and lipid levels.[47,60,62]

In a recent randomized, crossover study, a first of its kind, on the impact of the timing of food intake on human salivary microbiota found that eating the main meal late

inverts the daily rhythm of salivary microbiota diversity which may have a deleterious effect on the metabolism of the host.[67] In another clinical trial, gut microbial richness was significantly enhanced due to time-restricted feeding. Thus, it could be a safe remedy for the prevention of metabolic diseases related to dyslipidaemia, as it regulates circadian rhythm associated with gut microbiome modulation.[68]

In a trial among pre-diabetic sample, subjects were allowed to eat their meals in either a 6-hour time window near noon or a 12-hour time window for 5 weeks. The trial ameliorated the metabolic markers of diabetes without a significant reduction of body weight.[11] Individuals on a hypocaloric, three-meal-per-day diet lost more weight when the majority of the food was consumed in the morning, as compared to during the evening.[69] However, no significant changes in glycemia, insulin sensitivity, or respiratory exchange ratio (RER, defined as the ratio between the amount of carbon dioxide produced and oxygen used during breathing) were observed when obese, insulin-resistant men were exposed to a hypocaloric diet with food provided in the morning.[70] In another study that assessed the effects of 9-hour TRF, early (TRFe: 8 am to 5 pm) or delayed (TRFd: 12 pm to 9 pm) on glucose tolerance in men at risk for type 2 diabetes found that while only TRFe lowered mean fasting glucose, TRF improved glycemic responses to a test meal regardless of the clock time that TRF was initiated.[71]

In terms of safety, a recent study on the safety of time-restricted feeding, with 8-h feeding window/16-h fasting window daily, in 24 obese adults, with intervention for 12 weeks found that consuming food within an 8-h window can safely facilitate weight loss in subjects with obesity.[72] A recent review of the metabolic effects of intermittent fasting described when people took two or three meals within the feeding window, the one meal per day condition was associated with reductions in fasting glucose and improvements in LDL and HDL cholesterol. Even in one-meal condition, no mean deterioration in tension, depression, anger, vigour, fatigue, or confusion were reported.[73] Similar conclusions have been drawn in other studies.[74]

Even in cases related to cancer, fasting period of more than 13 hours resulted in lower risk of breast cancer recurrence compared to the subjects who fasted less than 13 hours.[75,76] Further, even in people suffering from metabolic syndrome and on medication have been found to benefit from TRF. A clinical trial found that TRF intervention improves cardiometabolic health for patients with metabolic syndrome receiving standard medical care including high rates of statin and anti-hypertensive use.[77] A meta-analysis of 19 studies found that TRF significantly reduced body weight and fat mass, while preserving fat-free mass. TRF also improved cardio-metabolic parameters such as blood pressure, fasting glucose concentration, and cholesterol profiles.[31]

In general, data from human clinical trials support the findings of animal studies. These include decreased body weight, lower concentrations of triglycerides, glucose, and low-density lipoprotein cholesterol and increased concentrations of high-density lipoprotein cholesterol.[78] Reviews of human studies suggest that a regular meal pattern including breakfast consumption, consuming a higher proportion of energy early in the day, reduced meal frequency (i.e., 2-3 meals/day), and regular fasting periods may provide physiological benefits such as reduced inflammation, improved circadian rhythmicity, increased autophagy and stress resistance, and modulation of the gut microbiota.[79] Studies also suggest that TRF might reset and synchronize metabolic "clocks" found throughout human body that may have got disturbed for various reasons including shift work, irregular sleep patterns, high stress, physical inactivity, obesity and frequent *ad libitum* eating. Thus TRF may provide an answer to cardiometabolic diseases often seen in high-stress occupations.[80] While further studies may provide additional insights, current research indicates that both the window of time spent eating during each day as well as the time at which food is actually consumed with reference to circadian rhythm are important to realize the beneficial effects of diet on healthspan.

## Conclusion and way forward

Multiple lines of evidence support the usefulness of *kalabhojanam* as optimal eating strategy that may result in long-term improvement in human health. Science is yet to reach a final and unequivocal conclusion and thus *kalabhojanam* needs to be further tested in human subjects, the evidence from a large number of animal-studies is unequivocal. Nevertheless, data from the available time-restricted feeding studies on humans, although limited, is supportive of the *kalabhojanam*. *Samhitas*, different scientific disciplines within health and medicine as well as experiential practice-based evidence are fully coherent in demonstrating the indispensable value of *kalabhojanam* for maintaining the metabolic health. Thus, food intake as suggested by Ayurveda and contemporary scientific studies, may be a simple, practical, and effective strategy to prevent many clinically relevant challenges including metabolic and non-communicable diseases. However, in translating these findings for better health among the masses, care must be taken that while *kalabhojanam* has definite elements of scheduled feeding but it is much more comprehensive than time-restricted feeding. Accordingly, it should be adopted in a comprehensive manner according to Ayurvedic insights presented in this analysis (Table 1).

This analysis also provides a novel method that may be useful in production of usable clinical knowledge. The future of Ayurveda lies in a fresh interpretation and coherent integration of known facts from *samhitas*, science and experience, and linking such integrated stock of usable knowledge to therapeutic and prophylactic actions on the ground. It would also be useful to have observational studies on various diet and lifestyle related non-pharmaceutical interventions in Ayurveda. Also, while *kalabhojanam* incorporates the time element of TRF but it is comparatively much more comprehensive (Table 1). Therefore, incorporating all the aspects of *kalabhojanam*, large-scale, long-term, multicentre clinical trials are required to determine the added health benefits and feasibility of implementing *kalabhojanam* in the general population on a daily basis to increase the potential translatability and acceptability. Additional areas of research include feeding schedule, *langhan*, *shodhan* and sleep regimes. It is difficult to replicate these strategies in animal models, so multicentre observational studies on humans may be the optimal solution.

Finally, this analysis has also uncovered interesting areas of research. Text placed in *agryasangraha* of *Charaka Samhita* requires a fresh interpretation in the light of contemporary research available on similar issues. In all the available translations and commentaries, it has been believed that the materials as well as non-pharmaceutical strategies included in *agryasangraha* are for the convenience and quick therapeutic reference. Our analysis, however, provides a different way forward. It is highly likely that *agryasangraha* contains drugs, strategies and guidance of indispensable value. Therefore, it would be worthwhile to explore strategies and materials included in *agryasangraha* in the light of the indispensability hypothesis for human well-being.

## Acknowledgements

This paper has greatly benefitted from the insightful suggestions by Prof. Dr. Kishor Patwardhan, Vaidya-Scientist Fellow; Professor, Department of Kriya Sharir, Faculty of Ayurveda, Banaras Hindu University, Varanasi, India. His contributions are gratefully acknowledged. We are also grateful to two anonymous reviewers for their useful suggestions.

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**Source of Support : Nil**
**Conflict of Interest : None**