



Review article

An Exploration on physiology of Vasa, Meda, Majja in Ayurveda w.s.r. to adipose tissue.

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ABSTRACT

Recent researches on adipocytes in human and mice model have reported that the adipocytes are not only the fat depots but having role in maintenance of physiology and metabolism through adipokines released by them in accordance to their anatomical location. Ayurveda scholars too have mentioned different tissues like Vasa (inter muscular fat), Meda (visceral fat) and Majja (bone marrow) which are predominantly rich in adipocytes similar to adipose tissues, with a different sites, functions, compositions and pathological outcomes. The metabolic effect of Meda and Majja Dhatu on other tissues like muscle (Mamsa Dhatu), bone (Asthi Dhatu) and reproductive tissue (Shukra Dhatu) shows their functional interdependence. The detailed description of therapeutic indications of Vasa and Majja under Snehakarma (oleation therapy) illustrates that clinical physiology of these tissues have been elaborated rather than general physiology. This article is an attempt to comprehend the physiological aspect of Vasa, Meda and Majja retrospectively on the basis of their therapeutic indication for the management of variety of disorders, in the form of Sneha through different therapeutic procedures. An effort has been also taken to distinguish Vasa, Meda, Majja based on the functional peculiarities of adipocytes present in different sites of body like omentum, muscle and bone marrow. Critical observation of explanations of Vasa, Meda and Majja in Ayurveda compendia and advanced research in field of adipocytes reflected that Ayurveda scholars had deep insights regarding the various dimensions of adipocytes, most of which are in consistent with the advanced physiology and biomolecular studies of adipocytes.

Keywords Vasa, Meda, Majja, Asthi, Snehana, adipocytes, tissue nutrition

INTRODUCTION

In recent past the adipose tissue has been considered as depot of extra energy but at present numerous researchers have documented a variety of homeostatic functions, along with functional peculiarities of adipocytes based on their distribution in different parts of body. Recent past researches have documented that adipocytes have endocrine functions and play a great role in regulation of numbers of physiological process like bone metabolism, immune mechanism, reproductive functions by releasing adipokines. Adipose tissue is basically a loose connective tissue comprised of mainly adipocytes including nerve tissue, stromovascular cells and immune cells (Kershaw EE and Flier JS, 2004) which are present in different places of the body. Ayurvedic scholars have mentioned distribution of Meda in different places of the body with different names like when it is present in small bones and abdomen i.e. around viscera called as Meda (visceral fat), in long bones is known as Majja (bone marrow) while intermuscular fat is termed as Vasa (muscle fat) (Sushruta Samhita Sharirasthana 4/12-13) and its role in maintenance of physiology and manifestation of diseases also. In Ayurveda, Meda and Majja have been considered as Dhatu (tissue) while Vasa as Upadhatu (subsidiary tissue) (Charak Samhita Chikitsasthana 15/16-17). They have not only identified different anatomical distribution but difference in their composition, quantity, functions and role in manifestation of different diseases (Table No.1), treatment modalities on vitiation etc. Although physiology and anatomy of these have not been elaborated much but applied physiology has been enumerated in detail by all Ayurvedic scholars under therapeutic uses as Sneha in different disorders, as per Dosha and seasons etc. Any disturbance in normal status of Dosha, Dhatu and Mala leads to pathology (Charak Samhita Sutrasthana 9/4) and for the maintenance of homeostasis, application of treatment modalities has been described based on principle of homologue and analogue(Samanya Vishesha Siddhant) (Charak Samhita Sutrasthana 1/44, Charak Samhita Sharirasthana 6/9). For example in case of Meda Kshaya substances increasing Meda have been advised (Charak Samhita Sharirasthana 6/10). These all indicate that Ayurveda scholar had an insight regarding different dimensions of adipose tissue, many of which are still under current trends of research. This article is an attempt to comprehend the physiological aspect of Vasa, Meda and Majja retrospectively based on their description found under the management of a

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variety of disorders in the form of Sneha in different therapeutic procedures. Along with this we have tried to differentiate Vasa, Meda, Majja based on functional peculiarities of adipocytes present in different sites of body like omentum, muscle and bone marrow. Adipocytes present in different depots of the body exhibit different functions which can be understood through the metabolic interdependence of Vasa, Meda, Majja and patho-physiological pathways of diseases manifested by them.

S. No.		MEDA(adipose tissue)	MAJJA(bone marrow/brain marrow)	VASA(inter muscular fat)
1.	Description	Dhatu	Dhatu	Upadhatu of Mamsa
2.	Panchabhautika composition (Chakrapani on Sushruta Samhita Sutrasthana 15/8)	Jala(water)+ Prithvi(earth)	Jala (water)	Not described
3.	Sites (Sushruta Samhita Sharirasthana 4/12-13)	Cavity of small bones and abdomen (Udara), red bone- marrow (Saraktameda)	Cavities of long bone and skull bones (Mastakgata Majja)	Sneha or unctuousness of muscle (Shuddha Mamsa)
4.	Types	Deposited fat (Baddha) and circulating lipid (Abaddha Meda) (Charak Samhita Nidanasthana 4/7)	Red and yellow bone marrow(Rakta and Peeta Majja) in Bone and brain marrow (Asthigata and Mastulung Majja) (Ashtanga Sangraha Sharirasthana 5/33). Dalhan has described that skull bone marrow (brain) gets nourished by Tarpaka Kapha (Dalhana on Sushruta Samhita Sutrasthana 21/14)	-
5.	Quantity (Ashtanga Sangraha Sharirasthana 5/91)	2 Anjali	Majja (bone marrow)-1 Anjali, Mastulunga Gata Majja (brain marrow)-1/2 Anjali	3 Anjali
6.	Functions (Sushruta Samhita Sutrasthana 15/5,Ashtanga Sangraha Sharirasthana 19/3)	Provides unctuousness (Sneha), sweat (Sveda) Stability and nourishment of bones	Provides unctuousness (Sneha), strength (Bala) Nourishment of reproductive organ (Shukrampushti) filling of bone.	-
7.	Role in organogenesis (Sushruta Samhita Sharirasthana 4/31)	Rakta along with Meda forms kidney (~Vrikka) while Mamsa, Rakta, Meda and Kapha together forms testes (Vrishana)	-	-

Table 1. Physio-anatomical description of Vasa, Meda and Majja.

MATERIALS AND METHODS

A thorough screening of Ayurvedic literature has been done for the description regarding the Vasa, Meda and Majja in different contexts like Dhatu, Srotas, Dhatu Poshana, Snehapana etc. Most recent contemporary research articles related to adipose tissue were thoroughly screened in standard e-databases like PubMed, Science Direct, Web of Science, Medline plus by using suitable keywords like developmental origin, differentiation, endocrine functions and biochemistry of adipose tissue, leptin, adipokines, myokines, marrow adipose tissue, adipogenesis and osteoblastogenesis, adipogenesis and myogenesis etc. and incorporated for the possible relevant interpretations of Ayurveda description to explore the physiology of Vasa, Meda and Majja.

REVIEW AND DISCUSSION

Ayurveda scholars have identified different tissues which are the primary sites of fat (Sneha) as Vasa, Meda and Majja. Meda and Majja have been considered as tissue (Dhatu) while Vasa as inter-muscular adipose tissue under accessory tissue (Upadhatu) of muscle tissue (Mamsa Dhatu) (Charak Samhita Chikitsasthana 15/16-17). Considering therapeutic significance,

Majja and Vasa are also enumerated as Sneha Dravya (substances predominant in unctuous property) of animal origin (Charak Samhita Sutrasthana 1/86). Their physio-pathological as well as therapeutic potential in different diseases have been also identified. As the physiology of Vasa, Meda and Majja has not been much elaborated but functions and role in physiological homeostasis can be ascertained from their therapeutic indication in reverse order (reverse pharmacology). For example, recommendation of Vasa in case of emaciation might be due to provision of direct nourishment to the muscles (Mamsa) and Meda. All these depiction associated with Vasa, Meda and Majja have been scrutinized and précised under following captions:

- 1. Physio-anatomical description
- 2. Panchabhautika composition
- 3. Distribution of fat in body
- 4. Nourishment and development
- 5. Difference in response to various factors
- 6. Different therapeutic indications of Vasa and Majja in Snehankarma (oleation therapy)
- 7. Functional aspects of Meda and Majja Dhatu
- 8. Interdependence of Vasa, Meda and Majja in physiopathological conditions

Difference in composition of Vasa, Meda and Majja

These adipose tissue depots also vary in terms of composition and metabolic point of view too. Ayurveda scholars have described difference in Panchabhautika composition of Meda and Majja which shows difference in lipid constituents in different fat depots as described in contemporary science. Petrus P et al, 2017 have observed difference in fatty acid composition and expression of lipogenic genes in SAT and VAT. Vagbhatta has further opined that properties of Vasa depend upon the site of muscle mass from which it has been extracted (Ashtanga Sangraha Sutrasthana 6/106-108) which might be indicative of difference in subcutaneous fat of different sites (Sbarbati A et al., 2010). Adipocytes in different depots show different endocrine functions. They exhibit uniqueness in expression and secretion of adipokine. IL-6, PAI-1 are

exhibited more in visceral adipocytes while leptin and adiponectin in subcutaneous adipocytes. Due to difference in expression of receptors, they do not have similar response to a particular signal. (Kershaw EE and Flier JS, 2004)

Anatomical positions of Vasa, Meda and Majja

The Sneha present in the body is named differently according to different anatomical position and functions (Sushruta Samhita Sharirasthana 4/13-14, Ashtanga Sangraha Sharirasthana 5/13). Contemporary science too had classified adipose tissue into different type on the basis of their location, origin, character-ization and functions. (Table 2) (Giralt M and Villarroya F, 2013; Scheller EL et al., 2015; Qiwen Li et al., 2018)

	Ayurveda Description	Contemporary description	
Adipose tissue	Sites	Adipose tissue	Sites
Vasa	Unctuousness of well-nourished Mamsa Dhatu (Shuddha Mamsa)		
Meda	Cavity of small bones and in abdomen (Udara)	Visceral white adipose tissue (VWAT)	Around the omentum, intestines, and perirenal areas accounting for 10% of total adipocytes of body.
		Brown adipose tissue (BAT)	Cervical, axillary, inter-scapular, and supra- clavicular regions
Majja	Cavities of long bone as Majja Dhatu and in skull bones are termed skull bone marrow (Mastulunga/Mastakagata Majja)		Ribs, sternum, vertebrae, and medullary canal of long bones (tibia, femur, and humerus)
Rakta Majja	Long bone	Red bone marrow /Regulated marrow adipose tissue (rMAT)	Interspersed within active hematopoietic sites such as mid- to proximal tibia, femur, and lumbar vertebrae
		Yellow bone marrow /Constitutive Marrow adipose tissue (cMAT)	Distal tibia and caudal vertebrae of the tail.

Table 2. Distribution of Vasa, Meda, Majja and Adipose tissue.

Difference in response to various factors

Subcutaneous and visceral adipose tissues are responsible for distinguished metabolic consequences by secreting adipokines. For example visceral adipose tissue plays more important role in manifestation of chronic low grade inflammation by secreting lower amount of beneficial adiponectin and higher level of pro-inflammatory factors. Due to this they are regarded as bad adipose tissue. They are more metabolically active and show increased lipolysis in response to catecholamine and decreased lipolysis in response to insulin and $\alpha 2$ adrenergic agonist activity. (Ma X et al., 2015;Bruun JM et al., 2005; Wellen KE and Hotamisligil GS, 2005)

These adipose tissues behave in a distinct way to the various influencing factors. For example central fat is increased by excess cortisol while subcutaneous fat is reduced by growth hormones, thyroid and estradiol increase brown fat adipogenesis while testosterone and cortisol reduce the differentiation of brown fat. (Ma X et al., 2015)

Similar observations have been documented in Ayurveda compendia as separate factors have been described for vitiation of Medavaha and Majjavaha Srotas. Factors vitiating Medavaha Srotas are lack of exercise, excessive day sleep, excessive intake of fatty things and alcohol (Varuni) while crushing, injury, compression of bone marrow lead to vitiation of Majjavaha Srotas .(Charak Samhita Vimanasthana 5/16)

Nourishment and Development of Meda Dhatu

Dhatu are nourished by Aahara Rasa and their nourishment is affected by both qualitative and quantitative status of Rasa Dhatu and previous Dhatu. Meda Dhatu and Vasa get nourished

by Mamsa Dhatu while Majja by Asthi Dhatu (Charak Samhita Chikitsasthana 15/16). This description of tissue nourishment may be understood by the common progenitor origin of myocytes and adipocytes. Common mesenchymal stem cells have two precursor i.e. lateral and paraxial mesoderm, from lateral mesoderm white adipose tissues are derived while from the paraxial mesoderm myocytes and brown adipocytes are derived (Park A et al., 2014).

During fetal and neonatal period development of skeletal muscles occurs though mesenchymal stem cells which entail three competitive process i.e. myogenesis, adipogenesis and fibrogenesis (Xu Yan et al., 2013). Conditions like maternal obesity may shift differentiation of MSC from myogenesis towards adipogenesis and fibrogenesis result in reduced number of muscle fiber and increased intramuscular fat (Min Du et al., 2010). Skeletal muscle plays a significant role in regulating fatty acid and glucose metabolism, thus any deviation in development of skeletal muscle during intrauterine life will cause disturbance in fat metabolism making the offspring more susceptible for type 2 diabetes mellitus and obesity. Recent studies have reported secretions of common adipo-myokines which forms adipose-muscle axis and modulates energy homeostasis in the body (Li F et al., 2017). Myokines released by contracting muscle have beneficial effect on glucose and lipid metabolism by enhancing glucose uptake and lipolysis. They also exert systemic effect on liver and white adipose tissue by regulating glucose and lipid metabolism (Oh KJ et al., 2016).

These phenomenon can be understood at the level of Agni

i.e. normal functional state of Mamsa and Mamsa Dhatvagni nourishes Meda Dhatu appropriately but on vitiation it disturbs the nourishment of Meda Dhatu. As per concepts of Ayurveda nourishment of succeeding Dhatu depends upon the previous one, so the nourishment of Majja gets affected by Asthi Dhatu (Charak Samhita Chikitsasthana 15/16). Previous studies have reported that Bone marrow adipocytes and osteoblast shares common precursor and affects genesis of each other. Its nourishment might be also affected by the Meda Dhatu too. A study by Bredella MA et al., 2011 suggested that visceral adipose tissues are positively associated with bone marrow But while describing therapeutic properties of Majja, it is mentioned that Majja increases Meda Dhatu also (Charak Samhita Sutrasthana 13/17). These explanations suggest the plasticity between marrow and visceral adipocytes (Pellegrinelli V et al., 2016).

Different therapeutic indications of Vasa, Meda and Majja in Snehana

Vasa, Meda, Majja are the constituent (Dhatu) of the body. They are also obtained from the different food resources be used in Snehana Karma. These Sneha Dravya have been categorized broadly into two types i.e. plant and animal origin (Charak Samhita Sutrasthana 13/9) and four types i.e. Ghrita, Taila, Vasa and Majja with the different therapeutic indications (Charak Samhita Sutrasthana 13/13). Snehapana is one of the therapeutic procedures employed in the management of various disorders. These Sneha like medicated Ghrita and oil have different indications in the form of oral intake (Paan), external oleation (Abhyanga), nasal drops (Nasya), enema (Basti) etc. in various disorders (Charak Samhita Sutrasthana 1/86). Although Vasa and Majja have been described under Sneha Dravya but they have different therapeutic indications (Table No. 3) as well as beneficial effects which show their different mode of action. As functional status of Dosha exhibits circadian rhythm, (Vandana V. et al., 2018) thus Snehapana has been also advised as per Dosha and circadian rhythm. Intake of Ghrita has been advised during autumn, Majja and Vasa during spring while Tail during rainy season (Pravrita). Sneha should be taken during night in conditions of Vata-Pitta excess and summer while during mid-day in excess of Kapha Dosha and winter. (Charak Samhita Sutrasthana 13/18-19). Recent studies on adipose tissue also reported that adipocytes present in different parts of the body have peculiarities in terms of functions and response to environmental cues. Selection of specific type of Sneha Dravya i.e. Vasa, Majja as per seasons and Dosha might be indicating circadian rhythm in fat metabolism. Recent studies have also proven that enzymes involved in fat metabolism behave differently as per circadian rhythm. Diurnal variations in metabolites of fatty acids, steroid hormones as well as acylcarnitine, glycerophospholipids and sphingolipids have been also reported. The studies show that circadian system plays an important role in regulating lipid metabolism pathways and genes involved in it are regulated by the core molecular clock, and their expressions are coordinated with rest-activity and feeding cycles. (Gooley J, 2016)

Ayurveda scholars have given an insight regarding influence of environment on peculiarity of adipocytes. They have quoted that Vasa (adipocytes) of marshy land (Aanupa Desha) possess warm potency (Ushna Veerya) while that of arid land (Jangala Desha) is of cold (Sheeta) potency (Charak Samhita Sutrasthana 27/295). Contemporary researches have also reported that on exposure to cold, there is increased browning of white adipose tissue as well as recruitment of BAT at their sites which results in enhanced thermogenesis and mitochondrial activity (Carpentier AC et al., 2018; Contreras C et al., 2015)

In obesity oral administration of Takrarishta i.e fermented preparation of butter milk which is a rich source of probiotics has been advised as obesity reducing drug (Medohara) (Charak Samhita Sutrasthana 21/22), which helps in regulation of lipid metabolism by enhancing the beneficial gut flora (Ghazalpour A et al., 2016).

Sneha Dravya	Indications	Possible mode of action
Vasa	Individuals having good tolerance for cold and wind, strong digestive power, dry and wasted body as a result of overexertion, decreased Shukra, Rakta, Kapha and Meda. Unbearable pain in bones, joints, veins (Sira), ligaments (Snayu), abdominal viscera (Koshtha) and vital organs (Marma), Vataprakopa (Charak Samhita Sutrasthana 13/47-49). It is also beneficial in piercing type of injury, prolapse, disorders of ear and head, nourishment of Shukra and enhances reproductive functions (Charak Samhita Sutrasthana 13/16).	Vasa increases Shukra, Kapha and Meda due to similar property like unctuous (Snigdha), heavy (Guru) etc. Its indication in case of prolapse suggests that it provides physical support to the organs. Fat of animal origin is rich in cholesterol helps in body building as well as synthesis of steroidal hormones such as sex hormones and vitamin D. Thus it maintains the reproductive functions and bone metabolism also.
Majja	Strong digestive power, able to bear stress, taking Snehaon a regular basis, afflicted with Vata Dosha, Krura Kostha(constipated bowel), those who require Snehana (Charak Samhita Sutrasthana 13/50). It enhances Kapha, Rasa Dhatu, Meda Dhatu, Majja, Shukra and strength (Bala). It increases the strength of bone specially (Charak Samhita Sutrasthana 13/17).	It enhances Rakta Dhatu as it helps in haemopoiesis (Wang H et al., 2018) and provides strength to bone. It shows that Majja affects the physiology of bone. It contains cholesterol which helps in synthesis of vitamin D. Recent researches have also shown that bone marrow adipocytes too not merely fills the bone but also act as endocrine organ and affects bone metabolism through their secretions. (Li Y et al., 2019) Previous studies have observed that adipose tissue derived from bone marrow induces spermatogenesis in azoospermic hamster (Karimaghai N et al., 2018) It has been also advised in case of Vata Prakopa which shows that it is beneficial in chronic disease conditions.

 Table 3. Therapeutic indications of Vasa and Majja in oleation therapy (Snehana)

Functional aspects of Meda and Majja

Meda and Majja Dhatu have been opined to play an important role in nourishment of bone and reproductive tissue. Their

imbalance state of physiology i.e. Meda Vriddhi and Majja Kshaya affects functioning of bone tissue and produces abnormalities (Sushruta Samhita Sutrasthana 15/ 9, 14,

Ashtanga Hridaya Sutrasthana 11/10-12, 18-19). These functions might be indicative of the role of adiponectin and leptin secreted by adipocytes in bone remodeling and reproductive functions. In short term conditions, bone growth is inhibited due to increased apoptosis and decreased proliferation while in long term regulation bone formation is increased by adiponectin (Qiwen Li et al., 2018).

Leptin also exerts effect on bone remodeling through local and systematic effect. It affects the secretion of neuroendocrine hormone which exerts effect on bone metabolism through hypothalamus. It increases bone density and enhances bone turnover through peripheral effect (Upadhyay J et al., 2015; Turner RT et al., 2013). In recent study, bone marrow adipocytes too have been found regulating bone homeostasis. (Li Y et al., 2019)

It has been also shown in mice model that leptin concentration affects sympathetic nervous system tone in brown adipose tissue. Increased concentration of leptin increases the tone of sympathetic nervous system in brown adipose tissue resulting in increased thermogenesis (Simonds SE et al., 2012). This effect can be understood as Vata Prakopa (aggravation of Vata Dosha) and increased functional state of Agni (digestive strength) in case of obesity. Leptin not only affects bone metabolism but also maintains the normal signaling of hypothalamus pituitary ovarian axis and helps in

reproductive maturation (Emily S. Jungheim et al., 2012). In diet induced obese mice model, it has been shown that hyperleptinemia due to obesity may result in central leptin resistance resulting in hypogonadism (Tortoriello DV et al., 2014). Obesity and increased BMI has been also linked with the adverse reproductive outcomes like decreased LH pulse amplitude, decreased excretion of progesterone metabolites altering follicular maturation and functions of corpus luteum resulting in menstrual irregularities chiefly due to anovulation (Jain A. et al., 2007). However in Ayurveda regulation of reproductive tissue has been explained as function of Majja Dhatu. Recent studies have reported evidence of induced spermatogenesis from bone marrow adipocytes in azoospermic hamster (Karimaghai N et al., 2018).

Interdependence of Vasa, Meda and Majja

Functionally they are interdependent to each other. Recent researches have also reported that various chemicals (adipokines) secreted by adipocytes present at different sites of the body help in functional regulation of tissues like bone, muscles and reproductive tissues as described in Ayurveda. (Fig.1) (Upadhyay J et al., 2015; Turner RT et al., 2013; Emily S. Jungheim et al., 2012; Oh KJ et al., 2016; Simonds SE et al., 2012)

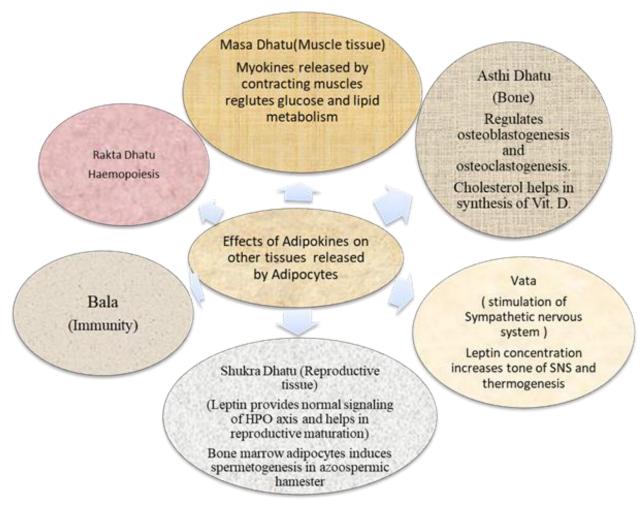


Fig. 1 Showing Interdependence of Adipocytes in Vasa, Meda and Majja with other tissues of the body.

SUMMARY

There are some similarities in contemporary and Ayurveda description regarding the various aspects of adipocytes. Both of them have mentioned maximum percentage of Vasa/ subcutaneous adipocytes, difference in Panchabhautika composition/fatty acid composition and lipogenic gene expression, similarities in terms of nourishment i.e. their nourishment level get affected by the skeletal muscle. Contemporary researchers have revealed that bone marrow adipocytes are not only the filler of bones but have important role in homeostasis of body (Horowitz MC et al., 2017). In Ayurveda too both Meda and Majja Dhatu have been shown to affect the homeostatic functions of the body. After analysis of various description related to physio- pathology in Ayurveda, the role of Meda Dhatu can be summarized as maintenance of energy homeostasis and metabolism, since the Meda Vriddhi results in manifestation of obesity and prodromal symptoms of Prameha ,while hypo-functional state results in emaciation especially in abdomen and flank region, affect the functioning of bone as its hyper-functional state results in (Asthi Kshaya), maintenance of cardiovascular functioning and normal thermogenesis as hyper functional status leads to cardiovascular disturbance and excess sweating.(Sushruta Samhita Sutrasthana 15/9,14 ; Charak Samhita Sutrasthana 17/68-70)

In the similar way the Majja Dhatu supports the functioning of Meda, Rasa, Asthi and Shukra Dhatu, regulation of functioning of Vata and Kapha Dosha as hypo-functional state leads to consistent nervous disorders, and regulates immunity or Bala in body respectively. Function of Vasa is to provide support to visceral organs as it is therapeutically beneficial in case of prolapse.

CONCLUSION

Although physiology of Vasa, Meda and Majja have not been much elaborated but there is a wide description of clinical physiology. Ayurveda scholars had deep insights regarding nutrition and metabolism of these tissues, as they have described about their constituents, functions, distribution, quantity, and separate vitiating factors for Meda and Majja, different therapeutic indication under Snehapana obtained from animal sources as per circadian rhythm, seasons and disorders. All these description are consistent with the recent advancement in physiology and biomolecular studies of adipocytes present in different sites of the body. Further scientific studies are required on the above description of Ayurveda for better understanding of role of adipose tissue in physiological homeostasis and pathophysiology of disorders too.

Future perspectives

By keen observation of therapeutic indications of Vasa and Majja under Snehapana, study can be planned to explore the functional aspects of adipocytes. Along with it distinct properties of different animal adipocytes have been described. Study can be planned to understand the variation in composition of Vasa and Meda obtained from diverse animal sources, which can be further utilized in management of various disorders.

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CONFLICT OF INTEREST

The authors have no conflicting financial interests.

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