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Dynamic Attributes of Lipid and Carbohydrate Interactions in Biosystems

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ABSTRACT

The article presents a perspective in the analyses of carbohydrate-lipid interactions in Biosystems as relevant to contemporary research and contemporaneous findings. It is necessary to elucidate the novel knowledge and information of organismal metabolism of carbohydrates and lipids.

Keywords: *Metabolism, pathways, insulin insensitivity, diabetes, thermodynamics*

INTRODUCTION

Carbohydrates and lipids constitute the energetic molecules and are principal components of the metabolic system. Carbohydrates are the major energetic molecules which are utilised by active tissue such as muscles and undergo conversion to lipid molecules for storage in the adipose tissue during starvation. Carbohydrate-lipid interactions are essential attributes in the control mechanism or regulation of energy metabolic system. As an instance, dietary fat influences glucose metabolism in salmon muscle that allows for a crucial dietary n-3/n-6 ratio in carbohydrate-lipid interactions which may be potentially significant to nutritionists in the development and improvement of energy yields in salmon feeding as a source for carbohydrates (1), and other extant variables and parameters in the regulation of body homeostasis, insulin resistance, diabetes control [2] and exercise [3].

METHODS OF INVESTIGATIONS AND MEASUREMENTS

Diverse trajectories and modalities have been observed to elucidate the dynamics of interactions between lipids and carbohydrates. Investigation and analyses of the thermodynamics of carbohydrate-lipid interactions demonstrated the impacts of a carbohydrate series, such as monosaccharides, disaccharides and trisaccharides on the phase-transition characteristics of aqueous dispersions of 1, 2-dipalmitoyl phosphatidylcholine (DPPC) [4]. The temperature of the lipid major phase transition from gel to liquid-crystalline phase was substantially unaltered in the presence of carbohydrate. The free energy change, delta G of the transition was zero on addition of carbohydrate to aqueous solutions in the enthalpy delta H and the entropy of the melting DPPC. The results revealed the thermodynamic features of carbohydrate-lipid interactions regarding specific attributes of carbohydrates in aqueous solutions and erstwhile proposed hydrophobic interaction associations with hydrocarbon tails of lipids in aqueous dispersions [4]. Investigation of the interactions of six carbohydrates, viz: trehalose, glucose, sucrose, glycerol, inositol and raffinose with dry dipalmitoylphosphatidylcholine (DPPC)

was conducted via the usage of differential scanning calorimetry (DSC) and infrared spectroscopy (IR) to determine and explicate the mechanism by which these carbohydrates sustain the morphological and functional integrities of the dry membranes [5]. DPPC findings showed that trehalose modulated the principal transition temperature, Tmid of dry DPPC less than that for completely hydrated DPPC, and elevated the enthalpy of that transition greater than when there was addition of water. Findings from IR spectroscopy ostensibly revealed a potential interaction mechanism. A vast majority of these carbohydrates showed that the IR spectrum for DPPC depicted alterations identical to those observed with the addition of water to dry DPPC, and the asymmetric P-0 stretching band decreased in intensity. The magnitude in which the investigated carbohydrates influenced the integrated intensity of the band and the Tmid showed proportionate correlation with the potential of the carbohydrates in the sustenance of dry membranes. Furthermore, with DPPC, bands ascribed to -OH deformations in trehalose and other carbohydrates were depressed. It is suggested that the interaction mechanism between carbohydrate and lipid is associated with hydrogen bonding between -OH groups on the carbohydrate and the phospholipid phosphate head group, with the exception of glycerol that depresses dry DPPC Tmid, as well as myo-inositol with no impact on Tmid or the DPPC IR spectrum. Also, none of the carbohydrates could preserve dry membranes. Based on the IR spectroscopy and other detections on monolayer preparations, it is suggested that glycerol-phospholipid interaction is via a mechanism that differs from that observed with other carbohydrates [5].

The impact of 0-0.1M sucrose on the phase-transition attributes of 1, 2-dipalmitoy l-3-sn-phosphatidylcholine (1, 2-DPPC) was investigated using high-sensitivity differential scanning calorimetry at 0.1km/min scan rate [6]. Enhancement of the sucrose content culminated in a minimal but experimentally significantly increased temperature (Tm) of optimum excess of ostensibly specific heat (Cmax) and in delta T1/2 as the transition breadth at1/2 Cmax, with a slight reduction of circa 8-10% at 1.0M sucrose in contrast to 0M sucrose in the calorimetric enthalpy (delta Hcal) of the crystalline transition from gel to liquid. The calorimetric measures of the 1,2-DPPC pretransition were not palpably influenced by sucrose in the studied concentration range; rather a 1.0 degree centigrade temperature Tp elevation of maximal excess ostensible specific heat in 1.0M sucrose was detected [4, 6].

The thermophilic attributes of DPPC and natural glycophospholipids mixtures, such as galactoglyceramide, lactosylceramide, asialo GM1, sulphatide, GM3, GM1, GD1a, GD1b in dilute aqueous dispersions were studied using high sensitivity differential calorimetry encompassing the entire composition range. The DPPC pretransition was dissipated and the principal transition cooperativity reduced significantly glycosphingolipid at mole fractions less than 0.2. The full complement of systems depicted non-feasible temperature composition phase diagrams. The mono- and di-hexosylceramides were easily miscible with DPPC as the glycosphingolipid proportion was elevated. A minimal proportion of 1-6 molecules of DPPC per glycophospholipids molecule (GSL) were introduced in a homogeneously mixed liquid phase. DPPC domains which were immiscible with other admixture of GSL-DPPC phase that indicated negative cooperative phase were revealed as DPPC resulted in excess of a determined amount in the system. A sulphatide negative

charge or four asialo-GM1 neutral carbohydrate residues in the glycosphingolipid oligosaccharide chain culminated in phase diagrams in cooperativity of gel and liquid phases within an expansive temperature composite range. Systems presenting gangliosides indicated complex phase diagrams in excess of one phase transition, devoid in phase-distinguished domains of pure gangliosides species. The thermotropic attributes of systems with DPPC and glycosphingolipids correlated with their interactions in monolayers at the interface of air/water [7].

Investigation of cyclodextrins (CDs) and DPPC liposome interactions by means of differential scanning calorimetry (DSC) (6) showed that the changes in the enthalpy and phase transition temperature resulting from the gel-to-liquid of the liposome crystalline phase transition were determined respectively, in the presence of alpha-CD, beta-CD, gamma-CD, heptakis (2, 3, 6-tri-0-methyl_-beta-CD (TOM-beta-CD and 2-hydroxylpropyl beta-CD. The influence of the enthalpy change of the transition temperature was in the magnitude of DOM-beta-CD > alpha-CD>TOM-beta-CD. The residual CDs induced transient changes in the transition temperature and enthalpy. The sorts of interactions realised between CDs and DPPC elucidated the DSC curves in the presence of the aforementioned CDs. The DOM-beta-CD produced a soluble complex whereas alpha-CD produced an insoluble complex with DPPC liposomes, with merely an infinitesimal proportion of TOM-beta-CD traversing the liposome matrix [8].

The interactions of 3-0-methyl-mannose polysaccharides (MMPS) extracted from Mycobacterium smegmatis with a mixture of MMP-10, -11, -12, and -13 or derived by chemical synthesis as MMP-5(s), -8(s), -11(s), and naphthenic acid (NA) commercial mixture in aqueous solution at 25 degrees centigrade and pH 8.5 were quantitatively analysed by electrospray ionization mass spectrometry (ESI-MS) [9]. The association constants K (a) for MMP binding to four NAs of Myristic acid, palmitic acid, stearic acid and trans-parinaric acid were determined via indirect ESI-MS assay, the "proxy protein" procedure. The K (a) values ranged from 10^4-$10^5 M^{-i}$. The results derived from synthetic MMP and palmitic acid binding, increased with carbohydrate size. On the application of a competitive binding assay or the "proxy protein/proxy ligand" ESI-MS technique, it was demonstrated that MMPS specifically bind to NAs in aqueous solution, with ostensible affinities of circa $5x10^4$ M^{-1} for the NAs mixture. This demonstrated that MMPs are capable of binding to hydrophobic species which indicate more complexity than those having linear alkyl/alkenyl chains. Furthermore, this constitutes a potential modality to elucidate carbohydrate-lipid interactions [9].

The morphology and integrity of carbohydrate-lipid interactions was conducted using complexes of MMPs derivative and fatty acids (FAs) as model systems [10]. The reliability of solution affinities and gas-phase dissociation activation energies (Ea) on FA length elicited a pronounced attribute of carbohydrate-lipid interactions in the stabilization of MMP+FA complexes. Solution of 1H-NMR findings depicted feeble MMP methyl groups and FA acyl chain interactions with disordered complexes as seen by MD simulations FA methyl group, and contributions to the Ea were identical to n-alkane transfer heats from the gas phase to polar solvents, thus indicating that MMP binds ligands via dipole-interactions. The MD findings suggest hydrophobic interactions and H-bonds in association with the FA carboxyl group, and disordered gaseous complexes compared with collision cross sections of

deprotonated MMP+FA ions with MD [10].

Diverse pathogen-induced potential etiologic immune responses were measured via the interaction of a virulence factor inhabiting carbohydrates with host membranes. In order to decipher the basic nature of interactions between carbohydrates and lipids in molecular recognition, certain hybrid quantum mechanics/quantum mechanics (QM/QM) scheme was employed to probe the structural basis and energetics of carbohydrate-phospholipid interactions in two disparate phospholipids (POPC and DOPC) and mannose interactions using density functional theory (DFT) regarding competing interactions to water. The findings unravelled the intrinsic attributes of interactions extant between the carbohydrate and phospholipid system. The relevance of the OH…O, CH…O and CH…n interactions to maintain the intermolecular complexes are easily detectable. The measured mean interaction energies for the diverse carbohydrate-water-lipid complexes indicated that both mannose and water have predilection in interaction with POPC than DOPC. The invariable functionalities of hydrogen bonding and nonpolar interactions were relevant in the recognition and enhanced stabilization of carbohydrate-phospholipid complexes. The initial hybrid QM/QM strategy on carbohydrate-lipid interactions suggests that mannose with phospholipid interactions culminate in alterations of charge conformations and distributions; and a comparison of these QM energies with Molecular Mechanics (MM) dependent energies for the same interactions tend to be of advantage in defining the all-atom carbohydrate-lipid force field [11].

It is established that carbohydrates protect membrane structures against fusion and leakage. Dynamic light scattering (DLS) measurements demonstrate that carbohydrates significantly augment the average diameter of the phospholipid membrane of 1,2-dimyristoyl-sn-glycerol-3-phoshpocholine (DMPC) via the application of dynamic light scattering (DLS), transmission electron microscopy (TEM) and various spectroscopic methods [12] , This may indicate that carbohydrates are directly bonded to the lipid bilayer surface through effective interactions of hydrogen bonding. In nature, self-assembly processes of amphiphilic molecules are inextricably linked in the design of structures of higher order, such as cells, with resultant formation of well-defined capsules bonded by non-covalent forces. Hydrogen bonding in fructose promotes the self-assembly of hydrophobic molecules into well-organized structures [13].

REGULATORY METABOLIC EFFECTS IN INTERACTIONS

Respiration competition within substrates in the tissues of animals has been documented for circa eight decades. The most relevant quantitative interaction is that between fatty acids and glucose [14]. The Glucose Fatty Acid Cycle was demonstrated in 1963 elucidating a reciprocal metabolic association between glucose and fatty acids that is non-dependent. Glucose enhances glucose oxidation including glucose and lipid storage, with the inhibition of fatty acid oxidation. The presence of FFAs promotes fatty acid storage, inhibits glucose oxidation and propensity to enhance glucose storage during depletion in glycogen reserves. Inhibitory impacts of fatty acids on entire body glucose consumption and oxidation, particularly in muscles are evidenced in humans; and associated enzyme regulatory mechanisms have been fully and properly demonstrated. Evidence is also extant that fatty acid oxidation influences the inhibition of glucose oxidation and triggers

glucose formation in the liver under strict enzyme control mechanisms or regulation. The permissive functionality of fatty acids in insulin secretory response of islet beta-cells is markedly viewed as a protective mechanism for persistent availability of substrates in respiration [14]. Lipid oligosaccharides (LLOs) portend substrates of oligosaccharyltransferase (OSTs) which are enzymes in the catalyzation of the total transfer of glycan chain in M-glycosylation. Microsecond molecular dynamics simulations of LLOs depicted that parallel to the membrane surface, a plethora of carbohydrate residues interact with the membrane lipid head groups, while the pyrophosphate group (PP) linkages are embedded in the lipid head group with the isoprenoid chains in the bilayer correlating general similarities in dynamics, orientations and structures of the archaea, bacterial and eukaryotic LLOs [15].

Prolonged exposure of islet beta-cells to fatty acids perturbs the insulin secretory response to glucose; as observed in uncontrolled diabetes, but with no established proof that fatty acids effect in the decreased glycogen storage or glycogen deposition in non-insulin dependent diabetes mellitus [16]. Glucose storage inhibition that culminates in prolonged augmentation of plasma FFA in humans' in vivo and experimental animals is interrelated with glycogen repletion; and conversely, glucose storage inhibition in type 2 diabetes mellitus is linked with glycogen depletion. The precise functionality of fatty acids in impaired carbohydrate metabolism in type 2 diabetes provides the latitude for expansive future and continuous research. The fundamental attributes of lipid metabolism are linked with fatty acid oxidation in energy production or lipid synthesis or lipogenesis. Lipid metabolism is inextricably linked to carbohydrate metabolism which may undergo conversion to fat with a degenerative resultant impact in diabetes mellitus [17, 18]. Insulin, epinephrine, adipokines and diverse agonists stimulate pathways which regulate the actions of veritable enzymes connected with the metabolic regulation or control mechanisms for the integration of organismal lipid and carbohydrate macromolecules. Excessive food intake dysregulates these pathways with deranging features culminating in insulin resistance and type 2 diabetes mellitus [19, 20].

Carbohydrate and fatty acid utilization is perspicuously influenced from consumption and generation rates of high energy molecules in cardiac muscle. In optimally oxygenated cardiac tissue, fatty acids have is the preferred substrate by both in vivo and in vitro investigations. Availability of fatty acid diminishes glucose consumption via the inhibition of disparate steps in the glycolytic pathway. As a result of the inhibitory mechanisms of long- and short-chain fatty substrates and as the impact is eradicated in hearts perfused in anaerobic milieu, fatty acid oxidation is an ostensible requisite for this effect [21]. Increased energy appropriation in optimally oxygenated hearts, results in accelerated fatty acid and/or glucose consumption. Oxygen transport to the heart may be restricted either by diminishing to zero the perfusate oxygen tension with concomitant hypoxia or anoxia or by the limitation of perfusate flow with increased oxygen tensions to induce ischaemic events. These lead to suppression of fatty acid oxidation and stimulation of glycolysis in hypoxic and anoxic hearts. The flux acceleration via glycolysis may vary from 10- to 20-fold. On the contrary, ischaemia results inversely to a transient glycolytic flux elevation that is invariably accompanied in approximately five minutes by inhibition. Fatty acid oxidation is depressed in ischaemic hearts culminating in the

accumulation of long-chain Coenzyme-A derivatives and augmentation in triglyceride concentrations [21].

Carbohydrates and fats constitute essential fuels in aerobic exercise with reciprocal shifts in the availability of these macromolecules which undergo oxidation. The interaction between the oxidation of carbohydrates and fatty acids is dependent upon the intracellular and extracellular metabolic milieu. Substrate availability in both the internal and external dimensions of muscle, exercise intensity, exacting effect, exertion and duration govern these conditions [22, 23]. The provision of enhanced fat availability to downregulate carbohydrate metabolism in cardiac, diaphragm and peripheral skeletal muscle is well adverted in nature. The control of fat metabolism during intense exercise and accelerated carbohydrate provision in human skeletal muscle become more functionally elucidated recently. Studies have demonstrated the complexity of fat metabolism regulation with involvement of several regulatory steps, including fat transport into muscle cells, cytoplasmic fat binding and transport, control of intramuscular triacylglycerol synthesis and breakdown and fat transport into the mitochondria. The revelation of protein effects in fat transport traversing the plasma and mitochondrial membranes, and the potential of translocation to the membranes [12, 15] in exercise, and the new-fangled trends and functionalities of adipose triglyceride ligase as well as hormone-sensitive lipase in the regulatory or control mechanisms involved in skeletal muscle lipolysis are instances of contemporary. The information and knowledge are amenable in the proposition of mechanisms to elucidate fat metabolism downregulation in the event of mitigating carbohydrate availability in the shift from slight to moderate, with concomitant exerting aerobics exercise [3, 24].

DISCUSSION

Carbohydrate and lipid macromolecules are large molecules within Biosystems which function in vital physiological roles in energy metabolism; and also include proteins and nucleic acids which display numerous similarities and unique disparities. Carbohydrates and lipids are the energetic molecules, and constitute the major entities of the metabolic system. Carbohydrates are normally converted to lipid molecules and stored in the adipose tissue during starvation. Therefore, carbohydrate-lipid interactions are veritable attributes in the control mechanism or regulation of energy metabolic system. Varieties of lipids are extant but the lipids which ingress glucose catabolic pathways are cholesterol and triglycerides. Lipids are formed and broken down via steps of the catabolism pathways. The concentrations of cholesterol and lipids in the blood may be altered by interchanging of complex carbohydrates present in the diet [24] with resultant diabetes and insulin resistance pertaining to the diet [19], hypercholesterolemia and atherosclerosis are influenced by the variety of carbohydrates, fats and cholesterol.

The impacts of dietary carbohydrates and lipid contents on growth performance, feed consumption, carbohydrate and lipid metabolism are important to living organisms [25]. However, chronic lipidaemia and hyperglycaemia characterize type 2 diabetes which may be causal or contributory factors in beta-cell dysfunctionality via "glucolipotoxicity" [26].

CONCLUSION

This paper attempts to discuss the quantitative and qualitative analyses of the dynamics of carbohydrate-lipid interactions. Measures need to be developed, improved and adopted for the expansive determination of the reliability,

specificity and precision whereby veritable molecular events emphasize profound complexities and integrity of molecular interactions, as they allow for the investigation of macromolecular interaction. It is imperative to elucidate the novel knowledge and information of organismal metabolism of carbohydrates and lipids as well as the physiological relevance of insulin action and insulin receptor in metabolic functions in how they are influenced by normal and aberrant nature of the diabetic ambient.

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