BERMUDA TRIANGLE IN CHEMISTRY

ABSTRACT. It is believed that the place called Bermuda triangle is able to hide of human seeing objects entered its area. A Bermuda triangle in chemistry is able to hide (mask) atoms or planar molecular fragments cut by their mirror plane of symmetry, not of human eyes but, of polarized light. A triangular skeleton (frame) has been imagined, possessing the ability to cover many hundreds of molecular formulae, providing the latter refer to aliphatic, or partially aliphatic, compounds, and with a low degree of oxidation. This skeleton (frame) is based on a very general and strong principle, valid in *meso* entities. The idea is advanced that isomers coming up from a molecular formula could be of four types (groups): *meso*, C_2 symmetrical (*CTS*), *irrechi* (from *irre*gular *chi*ral) and *constitutional* (*constit.*). The following universal rule is revealed: all *CTS* and *irrechi* can be converted to *meso* ones, but the reverse is not true, at least for the same skeleton. At the same time, an impressive number of constitutional natural or synthetic combinations are characterized by at least one real or envisaged *meso* isomer. Thus, from a structural point of view, *meso* isomers are justified as reference compounds. The above mentioned principles have been applied to numerous natural compounds: amino acids, lipids, carbohydrates, nucleosides, vitamins, steroids, alkaloids, hydrocarbons. A mathematical equation sustaining the triangular representation has been proposed. One raises the question which of the four types is the upper. A tentative answer is given to this question.

Key words: Bermuda triangle, isomers, meso, C_2 symmetrical (CTS), diastereomeric chiral (irrechi), constitutional, comparative chemistry, integrative, duality

1. Introduction

The analysis of isomerism phenomena as well as of numerous natural and synthetic compounds disclosed at most four types of isomers: (A) *meso*, (B) C_2 symmetrical (*CTS*), (C) *irre*gular *chi*ral (*irrechi*) and (d) *constitutional* (*constit.*). We have tried to check an old idea [1,2], concerning the ubiquitous existence of symmetry in nature, especially in physical-chemical and biological systems. We have undertaken an integrative approach based on molecular formula, and an exercise of comparative chemistry, by using *meso* compounds as structural references. Every molecular formula concerning natural or synthetic compounds, with a significant moiety of an alkane skeleton, and a given level of complexity, might produce the afore mentioned four types (groups) of isomers. In fact, the significance given by us to the four types will become quite obvious from their use and application.

(A) *Meso* isomers. There are three types of *meso* compounds [3]: (**A1**) characterized by a mirror plane of symmetry; at their turn, (**A1**) are of two types: (**A11**) the molecule of the first type is formed of two enantiomeric chiral halves uniformly linked with each other [4-6]; (**A12**) the two enantiomeric chiral halves of the second type are uniformly linked on an atom or on a matrix devoid of handedness, or a matrix characterized by a mirror plane of symmetry [7]; (**A2**) The second type of *meso* compounds is devoid of elements of symmetry (dissymetric compounds) and they have to be analyzed by Cahn-Ingold-Prelog rules [8,9]. Their molecule contains two sets of asymmetric carbons with opposed handedness. (In the latter case one can assert that molecules are formed of two imaginary enantiomeric halves separated by an imaginary mirror plane of symmetry).

Meso isomers are optically inactive (optinactive) due to an internal compensation. The existence of two enantiomeric sides in *meso* compounds was proved by Fischer and Hertz [10] in an elegant experiment on galactaric acid. They kinetically reduced this acid and the product was a racemic mixture of galacturonic acids. The two enantiomeric acids were

separated as strychnine salts and characterized. In this way the internal enantiomorphy of *meso* derivative become externalized. Subsequently, chemists would try to overturn this feature of *meso* compounds and to predominantly, if not exclusively, prepare one product only [11-14].

Meso heterodimers polyols discovered (or invented) by Fischer – xylitol [15], ribitol (adonitol) [16], xylaric (trihydroxiglutaric) acid, ribaric acid [17] – have been a trailblazing achievement and they turned out to be models for other combinations of the same category. Mirror plane of symmetry has to be regarded as an intrinsic property of *meso* compounds. It should be considered both a physical instrument and a natural phenomenon. Mirror plane of symmetry cuts either a bond (bonds) or atoms. Relative to polarized light, mirror plane of symmetry transforms a heterodimer into a homodimer. Mirror plane of symmetry hides (masks) the atoms cut by it from polarized light, and what remains, as evidenced by this physical instrument, is an entity containing an even number of atoms, i.e. a homodimer. *Meso* heterodimers constitute a chemical duality, the two opposed sides of duality are their heterodimeric character, on one hand, and their expression as homodimers, on the other hand. According to Kelvin and Prelog theory [18-20] *meso* compounds are internally heterochiral. There is a fundamental difference between the mirror plane of symmetry in macrocosmos and at physical-chemical level in microcosmos. In the first case, the mirror plane of symmetry just indicates the limit of the two enantiomeric halves. At physical-chemical level, it can cut atoms and hide them of polarized light. As will be evident of this paper, this spectacular property of mirror plane of symmetry plays an extremely important role in systematization of isomers emerging of the same molecular formula.

(B) ***C_2 symmetrical* (*CTS*)** compounds have been defined in relation with an axis and a rotation of 180°. After this maneuver the same atoms should be regained as initially [21-23], and all *CTS* compounds are chiral and optically active (optactive). Their molecule is either formed of two identical chiral halves uniformly linked with each other [24,25] or of two identical chiral halves uniformly linked on an atom [25] or on an achiral [25] or *CTS* matrix [26]. According to Kelvin and Prelog theory [18-20], *CTS* formed exclusively of two identical chiral halves are homochiral with each other and internally homochiral [23,27]. Of this reason, they could be named also *twin* molecules [1]. The exceptional properties of *twin* (*CTS*) compounds were also noticed by Vickery [28]. Homodimeric *CTS* compounds constitute a chemical duality, the two opposed sides of duality are optical activity, on one hand, and their symmetry, on the other hand. There is one universal rule concerning *CTS* compounds: every member of this group possesses a real or imaginary *meso* isomer. Two cases should be mentioned. Compounds based on 1,2-diamino-cyclohexane [13,22,29,30] are *CTS* as long as they are trans. Their cis isomer should be *meso* only by adopting a planar cycle, as for allo-inositol. Of the six *meso* isomers of inositol [31,32], five are characterized by 1,4 mirror plane of symmetry, while allo-inositol is devoid of such a plane. Its *meso* nature ca be explained only by a planar structure, hence the mirror plane of symmetry cuts two opposed bonds. (One can write a *meso* isomer of 1,2-diamino cyclohexane as 1,2-cyclobutane derivative).

The first *CTS* combinations, the two enantiomers of tartaric acid, have been separated by Pasteur (1848) by crystalization from a racemic mixture that had been prepared by Kestner (1822) [33-35]. Pasteur noticed two types of crystals, that were enantiomorphic with one another. He separated the two types of crystals and found out that their aqueous solutions were dextrorotary and levorotary, respectively. Dextro-tartaric acid had been discovered by Scheele (1770) in the sediment deposited in the vats during the grape juice fermentation [36,37]. Another isomer, devoid of optical activity and not cleavable by any chemical or biological method, was discovered also by Pasteur (1853) and called *meso*-tartaric acid [33,34]. Stereochemical theory of tetrahedral and asymmetric (chiral) carbon atom [38,39] led van't Hoff to molecular models based on tetrahedrons which unequivocally represented every chiral carbon atom. By constructing and using these models, van't Hoff expanded the idea of enantiomorphism from crystals to molecules. (Dots and wedges representations of

today come from van't Hoff's models). However, at that time no scientist could rationally associate structural models with the two enantiomers [40]. In fact, the discovery of Pasteur increased the dilemma of representation, i. e., the relationship between a sample of an optically active compound and the unique, characteristic, structural model possibly assigned to it. This dilemma was solved by X-ray diffraction, i. e., of zirconium Kα rays, by sodium rubidium tartrate of the dextrorotary species, and the obtained model was assigned to (+)-tartaric acid [41]. By an impressive coincidence, this configuration of (+)-tartaric acid had been hypothetically attributed by E. Fischer (1896) [42]. Configuration of chiral centers of (–)-tartaric acid became also known, by the virtue of the law of enantiomorphism. Configuration of the two enantiomers has been connected with other chiral compounds, beginning with (–)- and (+)-glyceraldehyde [43]. A chemical relationship has been found between E. Fischer and his son, H. O. L. Fischer [44,45], due to a derivative of D- and L-mannitol prepared by the latter, i.e. 1,2-5,6-di-O-isopropylidene mannitol (*CTS*). By integration of finding of H. O. L. Fischer in the strategy of E. Fischer, structure elucidation of linear aldohexoses becomes more direct [46].

(C) ***Irrechi***. The third subgroup of isomers of *meso* compounds are also chiral and they are characterized by a molecular skeleton identical to *meso* and *CTS*, i.e. a phenomenon of isoskeletomeric relationship [47]. Still, chiral carbons are irregularly distributed in their molecule [48]. E. g. glucitol [17], bicubebin [49], bismurrangain [50], hybocarpone [26], asarolignans [51], larreatricin [52], numerous carotenoids [53,54]. *Meso* isomers are characterized by a 1:1 ratio of numbers of R and S carbons while in *CTS* ones this ratio is n:0, 0:n or 1:1. In *irrechi* combinations the ratio R/S has other values.

(D) ***Constitutional*** (positional) (*constit.*) isomers form the fourth group. They are isomer with the preceding ones but their skeleton is different. They are either optactive or optinactive. With relatively few exceptions, compounds currently met in living things are constitutional isomers. They are probably the most abundant in natural materials.

An interesting group of *constit.* isomers is formed by a non-uniform linkage of monomers: quadrigemine C [55], aspergilazine A [56], penicillixanthone A, phomoxanthone B, dideacetylphomoxanthone B, rugulotrosin B [57], quadrigemine B [55], taondiol dimer [58,59], numerous carotenoids [53,54].

The application of our systematization to monosaccharides, discovered/invented by Fischer and others, produces the following results. (**A**) *meso* monosaccharides: galactitol [(2S,3R,4S,5R)-hexitol] [15,60], allitol [(2S,3S,4R,5R)-hexitol] [61-64], galactooctitol [(2S,3S,4R,5S,6R,7R) octitol] [65-67], galactaric acid (2R,3S,4R,5S) [10], allaric acid (2R,3R,4S,5S) [68]. (**B**) *CTS* monosaccharides: D-mannitol [(2R,3R,4R,5R)-hexitol], L-mannitol [(2S,3S,4S,5S)-hexitol] D-mannaric acid [(2S,3S,4S,5S)], L-mannaric acid [(2R,3R,4R,5R)] [69], D-iditol [(2R,3S,4S,5R)-hexitol], L-iditol [(2S,3R,4R,5S)-hexitol], D-idaric acid [(2R,3S,4S,5R)], L-idaric acid [(2S,3R,4R,5S)] [70-72]. (**C**) *irrechi* monosaccharides: D-glucitol [L-gulitol (2S,3R,4R,5R)-hexitol] [73], L-glucitol [D-gulitol (2R,3S,4S,5S)-hexitol], D-glucaric acid [L-gularic (2R,3S,4S,5S)], L-glucaric acid [D-gularic (2S,3R,4R,5R)], D-altitol [D-talitol (2R,3S,4R,5R)-hexitol], L-altitol [L-talitol (2S,3R,4S,5S)-hexitol], D-altraric acid [D-talaric (2S,3R,4S,5S)], L-altraric acid [L-talaric (2R,3S,4R,5R)] [15,17,70,71,74] and 1,1,1,2,2,3-hexanehexol [75]. (**D**) *constit.*: D-hamamelitol [76-78]. Concerning limits and possibilities of reciprocal changing of types mentioned above, both *CTS* and *irrechi* can be transformed into *meso*. Some interesting facts should be mentioned: the molecule of iditols and idaric acids possesses an equal number of R and S carbons, similarly with galactitol, allitol, galactaric and allaric acids. However they are not *meso* but optactive [31]. The difference can be explained probably by the fact that the molecule of the former is formed of two identical chiral halves and the latter of two chiral enantiomeric halves. The two hydrogen atoms of central methylene of a *meso* derivative, i.e. 3-deoxyxylitol, 3-deoxyribitol, *meso*-diaminopimelic acid, etc., are not equivalent. If they are alternatively replaced by a hydroxy function, the products are different. The two central hydrogen atoms of *CTS* compounds, i.e. 3-deoxyarabinitol, 3-deoxylyxitol, L,L- and D,D-

diaminopimelic acid, etc., are equivalent: if they are alternatively replaced by a hydroxy function, exclusively one product is obtained.
The molecular diversity is connected with the following factors: (**i**) Structures as diamond [79], graphite and fullerenes [80,81] illustrate the best the ability of C atoms to bind with each other. However, all these forms present a very limited structural variety. (**ii**) What really confer molecular diversity to C combinations is the association of this element with hydrogen and this is evidenced by the remarkable molecular variety of aliphatic hydrocarbons [32,82,83]. Molecular diversity is a physical-chemical magnitude concerning the ability of a compound to present a large number of isomers. (**iii**) Chemical functional groups, in relative low proportion, also favor molecular diversity. (**iv**) Aromatic hydrocarbons present the lowest molecular diversity of all organic combinations. They contain an exceeding number of chemical functions, and they are in a state of advanced oxidation. In fact, they fill an intermediate place between elementary carbon and aliphatic hydrocarbons. Another remarkable feature of aromatic hydrocarbons is the fact that they do not present *meso* isomers. (**v**) Molecular diversity increases exponentially with molecular weight [27,83,84]. (**vi**) Carbon dioxide is a terminal facet of metabolism and combustion of organic compounds. It is characterized by a high chemical inertia. Carbon dioxide has to be attached to a preexisting structure, as a piece of metal in a lathe, and stepwise reduced, the energy of sun playing an essential role in this process called photosynthesis [85].
Our aim have been especially monomeric units [85], but we prove that compounds called by Metzler in this way can also have *meso* isomers, hence an authentic dimeric character.

2. THE MAJOR METABOLITES CONTAINING A SIGNIFICANT ALKANE MOIETY POSSESS AT LEAST ONE REAL OR ENVISAGED MESO ISOMER

A guiding line of this paper is to find out at least one *meso* isomer for every molecular formula. A serious obstructor to this is an advanced degree of unsaturation. E.g. is impossible to find out a *meso* isomer for $C_4H_4O_4$ (fumaric/maleic acids). However, $C_6H_8O_4$ (2,3-dimethyl derivative, etc) has a *meso* form [48,54] (Fig. 1). Similarly, every tentative to construct a *meso* isomer of benzene, fails.

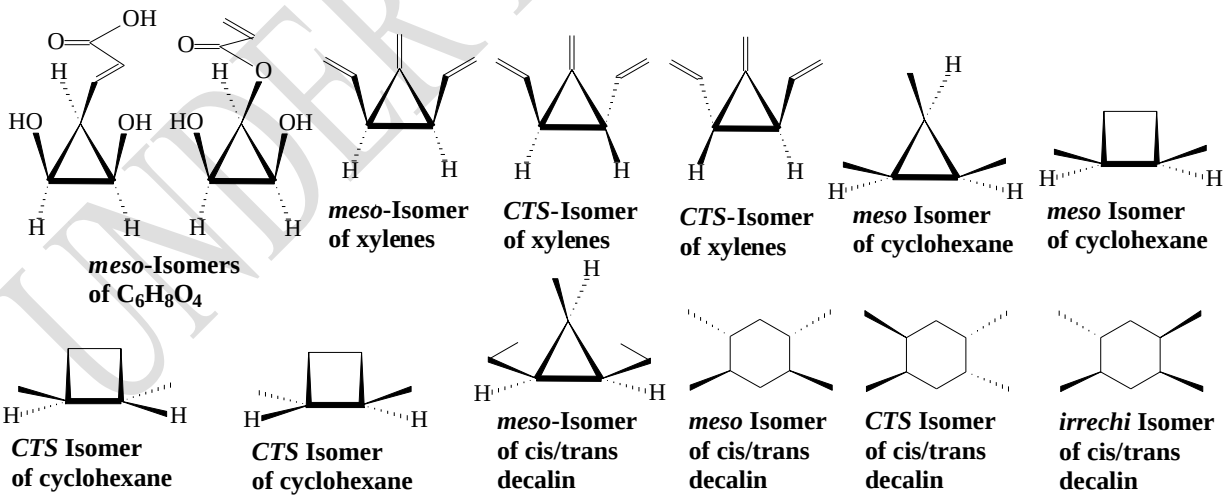

Figure 1. *Meso* isomers of unsaturated (fumaric/maleic acid), aromatic, and the latter's saturated compounds.

However, the thing is possible for xylenes, ethylbenzene, propylbenzene, etc. Also, reduction product of benzene, cyclohexane, presents meso isomers. Naphthalene, similarly to benzene, fails to give *meso* isomers, decalines instead presents such isomers (Fig. 1).

At least two dozens of isomers with molecular formula $C_3H_7NO_2$ can be written, just by utilising the consecrated valence of every component element. However, of the
envisaged isomers only some present elements of symmetry: two are *meso* (cis-1,2-dihydroxy-3-amino cyclopropane and cis-2,4-dihydroxy-azetidine), and two are *CTS* (trans-2,4-dihydroxy-azetidine, two enantiomers), and all the others, including (R)- and (S)-alanine, are *constit*.
In the following (Figs. 2-11), the envisaged isomers are presented for a large variety of natural and synthetic compounds.

2.1. Compounds with serial structure

Compounds with serial structure present a large variety of molecular formulas (Figs. 2-4), in agreement with their molecular weight.

2.1.1. Aliphatic hydrocarbons: alkanes, alkenes (cycloalkanes), alkynes (alkadienes)

Of aliphatic hydrocarbons, only alkanes fail to present a triangular *meso* isomer (Fig. 2). A tentative to evaluate molecular diversity of C_8H_{18} indicated 18 [84] or 19 (83) isomers. If one take into account optical activity [86], the total number of
isomers is 24 and 55, respectively. Of these, one is *meso*, two are *CTS* [87] (Fig. 2) and the others are *constit*. An unequivocal conclusion can be drawn: all alkanes beginning with C_8H_{18} present at least one *meso* isomer.
As a representative of C_nH_{2n}, eicosene can be seen (Fig. 2). The first term according to our reasoning is the *meso* isomer, cis-1,2-dimethyl cyclopropane [88].

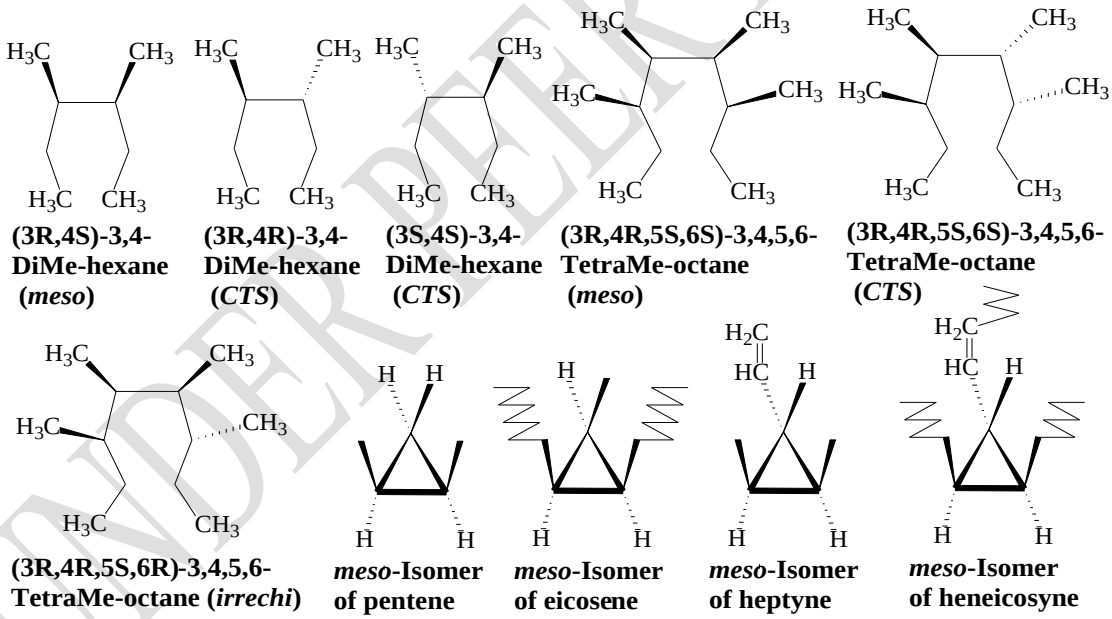

Figure 2.*Meso* isomers of saturated and unsaturated hydrocarbons.

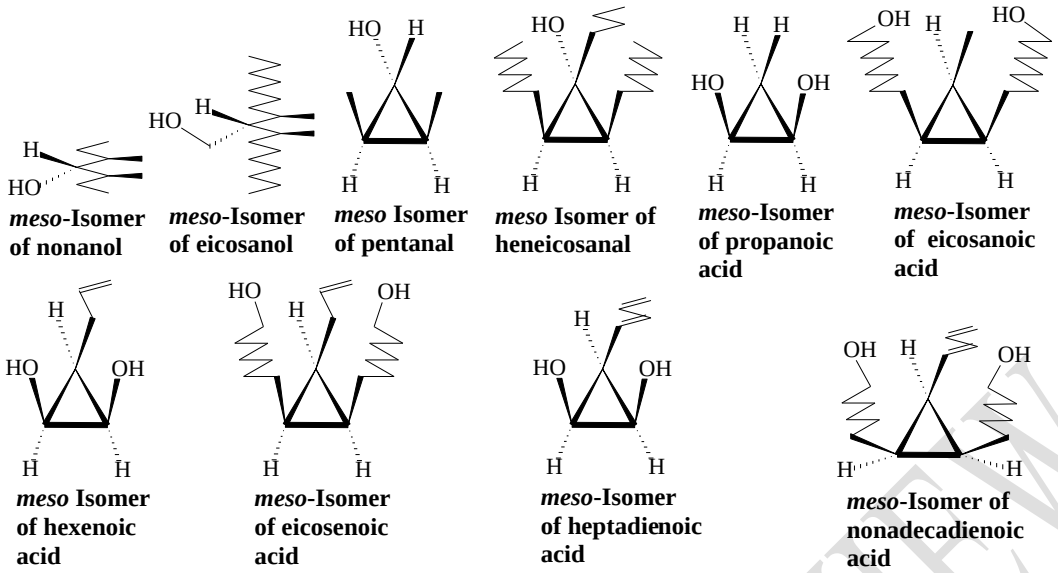

Figure 3.*Meso* isomers of some serial compounds with functional groups.

For C_nH_{2n-2} (alkynes and alkadienes) *meso* isomer of heneicosyne (as cis-1,2-dihexyl-3-hexenyl-cyclopropane) is indicated, the first term being C_7, cis-1,2-dimethyl-3-vinyl cyclopropane or cis-3,5-dimethyl-1-cyclopentene.

2.1.2. Serial compounds with functional groups

For monohydroxylic alcohols there is a meso isomer of eicosanol (9-hydroxymethyl-8,10-dimethyl heptadecane), the first term is C_9 (3,5-dimethyl-4-hydroxy heptane) (Fig. 3). For aldehydes and ketones we introduce *meso* isomer of heneicosanal (cis-1,2-diheptyl-3-hydroxy-3-butyl), the first term is C_5 (cis-1,2-dimethyl-3-hydroxy-cyclopropane).
Meso isomer of eicosanoic acid [cis-1,2-bis(octanol)-3-methyl-cyclopropane] represents organic acids, and the first term is C_3 (cis-1,2-dihydroxy-cyclopropane). C_3 still, as well as C_4 and C_5 have three types of isomers only (*meso*, *CTS*, *constit.*), while C_6 and higher terms possess four (*meso* of C_6 is 1α,2α,3β,4β-1,2-dihydroxy-3,4-dimethyl cyclobutane). Monoenoic acids are symbolized by a *meso* isomer of eicosenoic

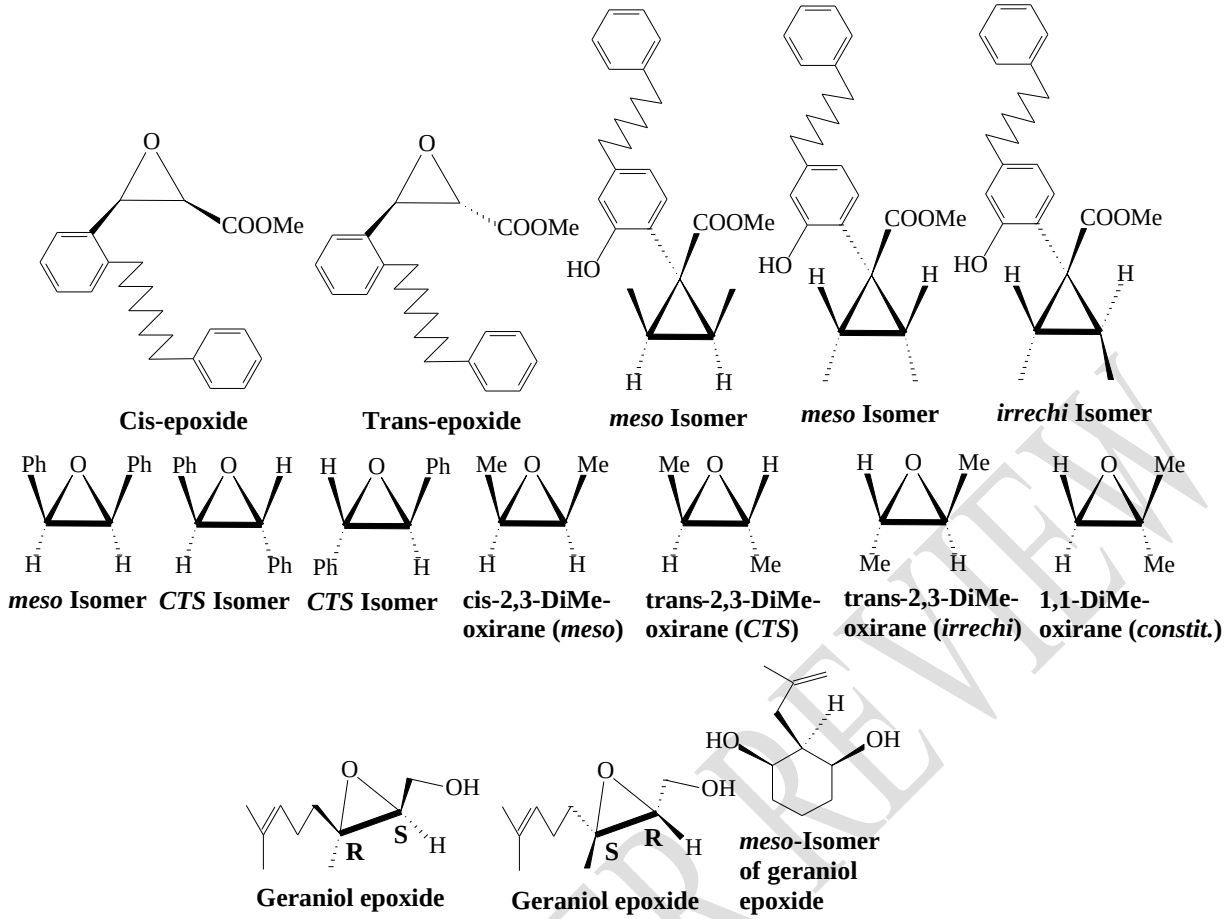

Figure 4.*Meso* isomers of some epoxides.

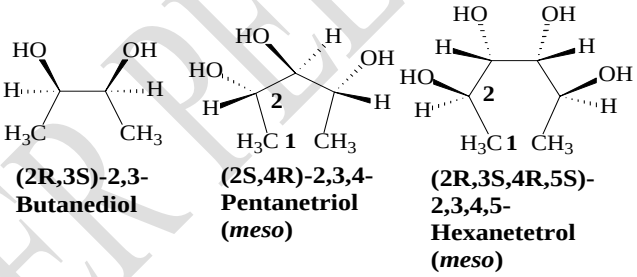

Figure 5. *Meso* isomers of diols, triols, tetrols.

acid [cis-1,2-bis(heptanol)-3-allyl-cyclopropane] and the first term is C_5 (cis-1,2-dihydroxy-3-allyl cyclopropane). The following isomers are considered *constit*., isomers of valproic acid (2-propyl pentanoic acid; $C_8H_{16}O_2$): 2-ethyl-3-methyl pentanoic acid, di-isopropyl acetic acid, (R)-2-isopropyl pentanoic acid, (S)-2-isopropyl pentanoic acid, octanoic acid [89]. According to our systematics, we have to begin with the finding of a $C_8H_{16}O_2$ *meso* isomer. This can be cis-1,2-dihydroxy-1,2-diethyl-3-methyl cyclopropane, cis-1,3-dihydroxy-2,2-diethyl-cyclobutane, 1β,2β,3α,4α-1,2-diethyl-3,4-dihydroxy
cyclobutane, or 1β,3β,4α,6α-1,3-dihydroxy-4,6-dimethyl-cyclohexane, or others. As can be seen from their structure, the latter three isomers present also *CTS* and *irrechi* forms. And the $C_8H_{16}O_2$ isomers mentioned earlier, valproic acid inclusively, are all *constit*. (see below). Dienoic acids are made up by the *meso* isomer of nonadecenoic acid [cis-1,2-bis(6,6'-hydroxy-hexane)-3-butadienyl-cyclopropane] and the first term is C_7 [cis-1,2-dihydroxy-3-(1-butadienyl) cyclopropane].

Epoxides. We have placed epoxides (Fig. 4) distinctively of alcohols and ethers since they are in a higher state of oxidation. The

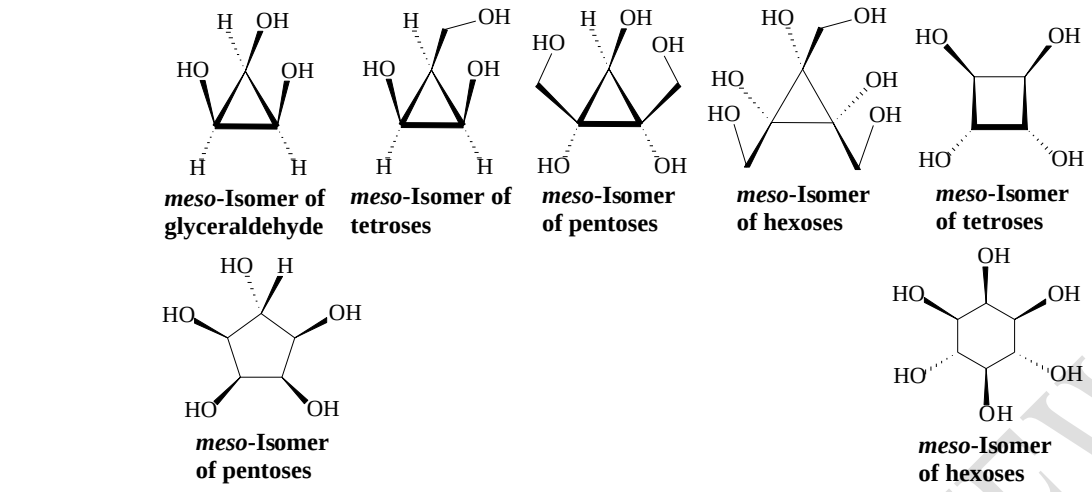

Figure 6. *Meso* isomers of aldoses and ketoses.

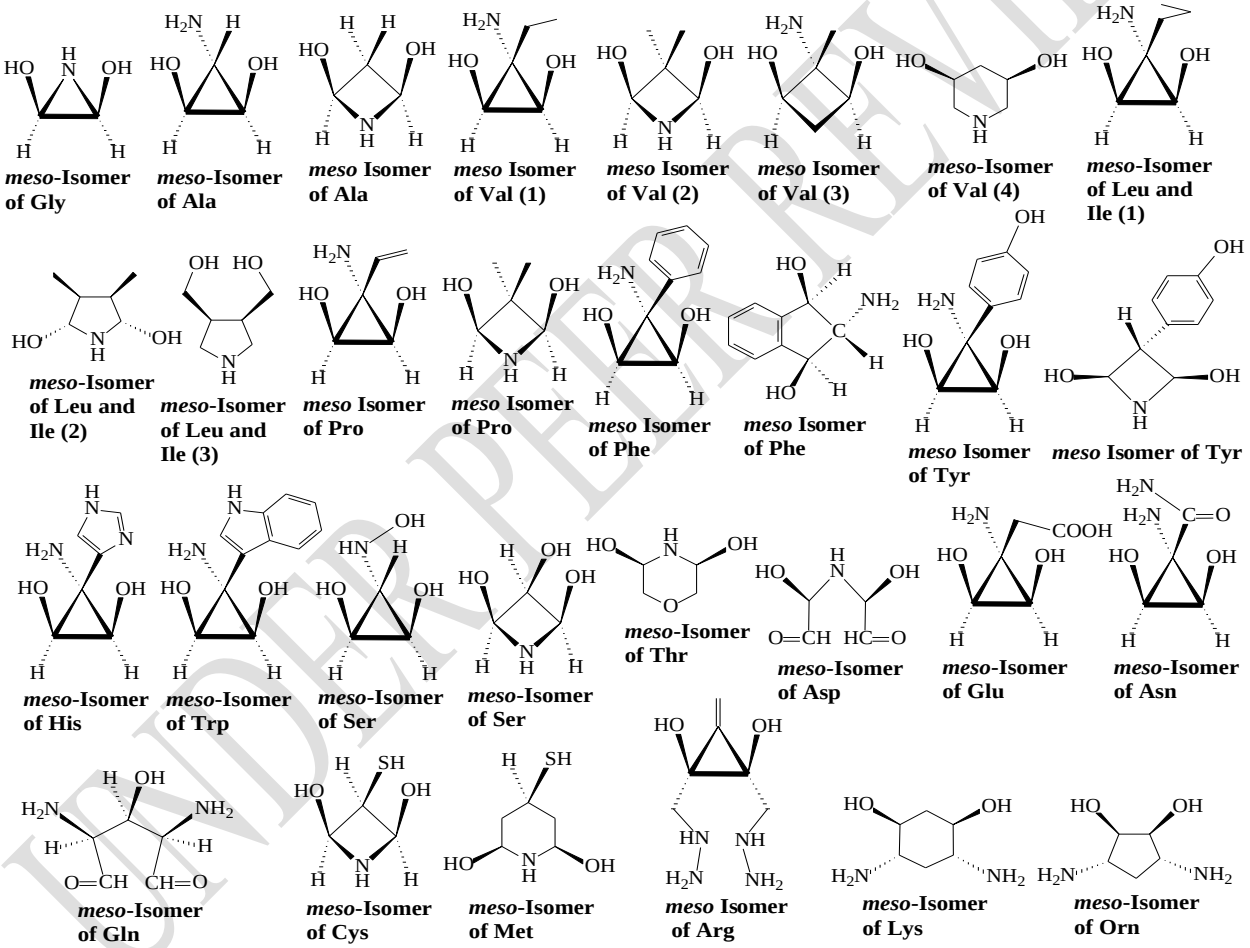

Figure 7. *Meso* isomers of the twenty fundamental amino acids. (see also text).

two epoxides (cis and trans) have been prepared and separated by chemists in Pennsylvania aiming at drugs intended to alleviate the symptoms of asthma [90]. We have imagined two *meso* and one *irrechi* isomers for the two afore mentioned epoxides. Hence the latter are *constit.* isomers as related to *meso* ones. The same authors describe three isomers of 1,2-diphenyloxirane (stilbene oxide), one *meso* and two *CTS*. Dimethyloxirane is illustrated equivocally [91], although it has four types of isomers: *meso*, *CTS*, *irrechi*, *constit*. Two enantiomeric geraniol

epoxides have been prepared [92], and we have imagned a *meso* isomer for them (Fig. 4), hence the two enantiomers are *constit*. isomers.

2.2. Natural compounds of biochemical interest

A general formula can represent diols, well exemplified by butane diols. As all the other compounds having two asymmetric carbons only, 2,3-butanediol has but a *meso* isomer and two *CTS*; 1,3-butanediol is a *constit*., isomer. Diols can present *irrechi* isomers only by contribution of alkane chain (see 3,4,5,6-tetra-Me-octane above). Triols, similarly to trimethyl alkanes (see 3,4,5-triMe-heptane) cannot have *CTS* isomers, but *meso*, *irrechi* and *constit.*; the first term is 2,3,4-pentanetriol. Tetrols presents all four types of isomers, the first term is (2R,3S,4R,5S)-2,3,4,5-hexanetetrol (Fig. 5).

A spectacular example of coexistence in natural materials of *constit*. and *meso* isomers in nature can be found in carbohydrate chemistry. *Meso*-isomers of aldo- and keto-pentoses ($C_5H_{10}O_5$) are 1,2,3,4,5-pentahydroxy cyclopentanes [93-95]. Aldo- and keto-hexoses ($C_6H_{12}O_6$) are represented by six *meso* inositols [31,32] (Fig. 6).

Biochemical compounds also present *meso* isomers (Figs. 2-11). Saturated, mono- and polyenoic fatty acids are represented by the isomers of stearic acid, oleic and eicosapentaenoic acid (the famous omega-3). As is obvious, an isomer of $C_{18}H_{36}O_2$ (cis-1,3-dihydroxy-cis-4,6-diheptyl-cyclohexane) present all four type of isomers: *meso* (cis-1,3-dihydroxy-cis-4,6-diheptyl-cyclohexane), *CTS* (as pairs of enantiomers) (trans-1,3-dihydroxy-trans-4,6-diheptyl-cyclohexane, etc.), *irrechi* (cis-1,3-dihydroxy-trans-4,6-diheptyl-cyclohexane, etc.) *constit*., (stearic acid, etc.). A general formula has been elaborated for mono- and polyunsaturated fatty acids [96].

Compounds with a ubiquitous distribution in living matter, the twenty fundamental amino acids are characterized by an unequaled structural variety. However, without any exception, they present *meso* isomers (Fig. 7). These amino acids are met especially integrated in proteins and in this state they manifest themselves by their tails [85]. *Meso*, *CTS* and *constit*. isomers present the following amino acids: Gly, Ala, Val, Thr, Asp, Pro, Phe, Arg, Trp. *Meso* and *constit*. isomers present the following amino acids: Tyr, His, Ser, Glu, Asn, Gln, Cys, Met. Leu, Ile, Lys and Orn present all four types. Amino acids containing an aromatic fragment and/or a relative high level of chemical functions are more limited in structural variety. However, we have had again the opportunity to exploit the planar character of benzenoid structures.

For long chain bases (LCB) (sphingosines), LCB d18:1 (Fig. 8) has been selected. *Meso* isomers have been also found for LCB t16:0, LCB d16:0, LCB d16:1, LCB t18:0, LCB t18:1, LCB t20:0, LCB t20:1. *Meso* isomers of saturated LCB should use *meso* isomer of nonanol as a model. Nucleosides, nucleotides and their deoxy counterparts are represented by adenosin and deoxy-adenosin. All prostaglandins have matching *meso* isomers, as indicated by PGE1, PGF2α, PGE2, PGF3α. All natural and synthetic alkaloids have *meso* isomers, providing they include a significant alkane moiety e.g. piperidine, piperazine, etc. Camphor is also present. Practically, all hydrosoluble vitamins present *meso* isomers. A component of coenzyme A, pantoic acid, has pentahydroxy cyclohexane as a *meso* pair (Fig. 8).

Squalene presents at least one *meso* compound. Sterols have been exemplified by cholesterol, stigmasterol, sitosterol, campesterol, ergosterol and digitoxygenin (Fig. 9). Digitoxygenin also presents the four types of isomers. A similar solution has been found for estrone, C_{19} (5α-androstanolone), C_{21} (prednisolone, 11β-Hydroxy-progesterone, pregnenolone, progesterone, corticosterone, cortisol, aldosterone), C_{24} (biliary acids: cholic, chenodeoxycholic, deoxycholic, lithocholic). All lipophilic vitamins – A, D, E, K – present *meso* isomers (Fig. 10). Vitamin E is represented by α-tocopherol and α-tocotrienol, but all members of this vitamin have *meso* isomers, and the same are vitamins K1 and K2. Both *meso* isomers of vitamin K1 and K2 are indicated. The planar structure of benzenoid compounds has been succesfully used in *meso* isomers of the following: biopterin (cis-2,4-dihydroxy-3-methyl-3-adenin oxetane), biotin [cis-2,4-dihydroxy-3-propyl-3-(3,4-diamino-thiophene-2)oxetane], adenosin (cis-3,4-dihydroxy-cis-2,5-dihydroxy-1-adenin cyclopentane), $FADH_2$, $FMNH_2$, and even coenzyme A. In order to

write *meso* isomer of $FMNH_2$ we extracted an O atom from a keto bond, however leaving redox system intact. An excellent alternative to this is to link the isoalloxazine system and a phosphonic (not phosphoric!) on C-3 of ribitol.

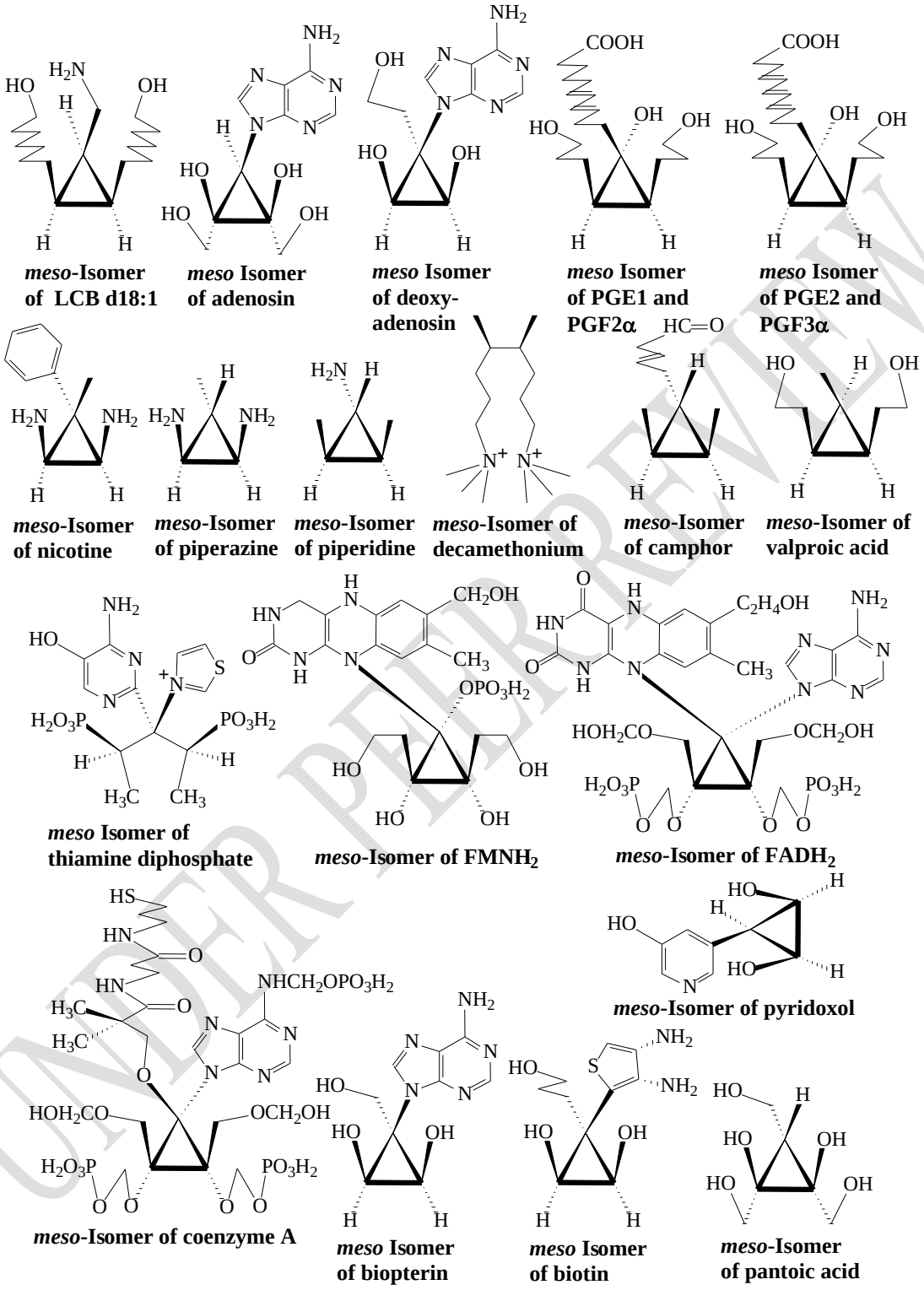

Figure 8. *Meso* isomers of some natural compounds, including hydrosoluble vitamins.

3. Triangular representation and mathematical equation

A mathematical equation and a triangular representation [96] (Fig. 11) have been imagined to illustrate *meso* isomers. In equation n–3=2x+2y+z+w, n is the number of chain forming atoms, x,

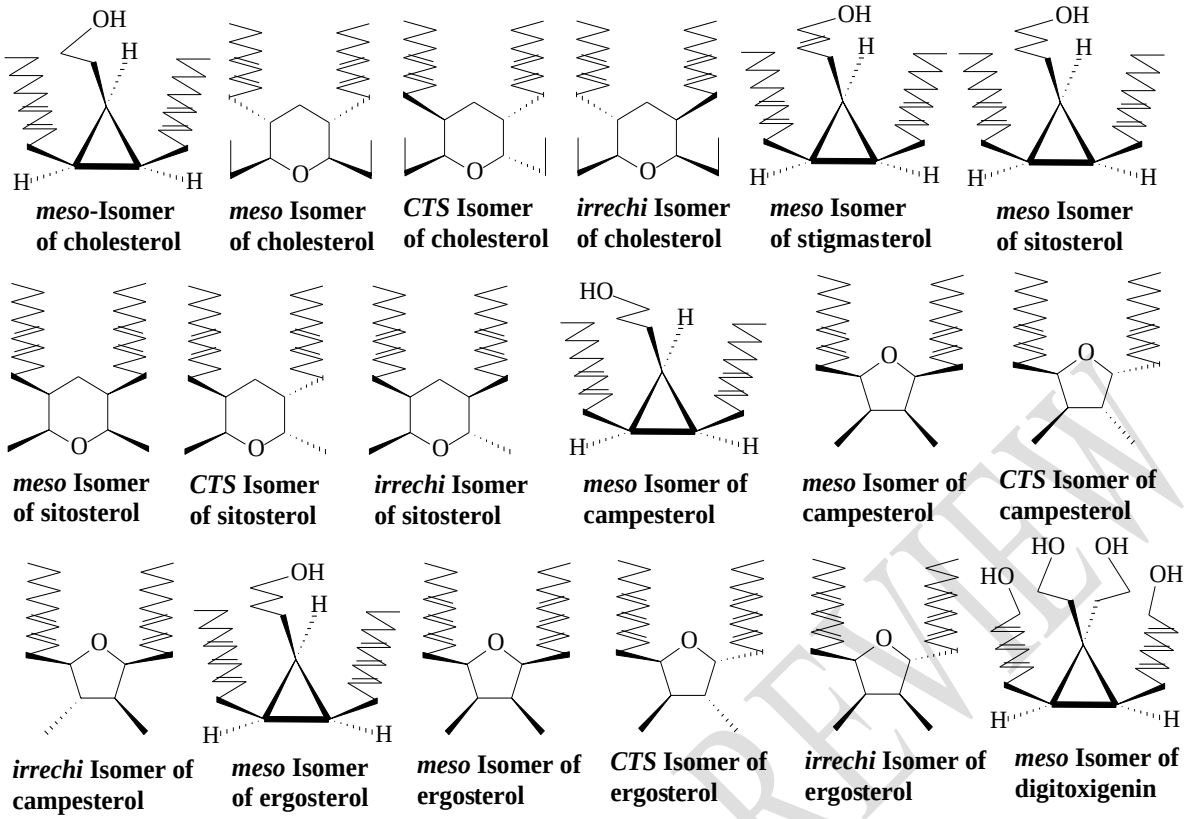

Figure 9. *Meso* isomers of some natural sterols.

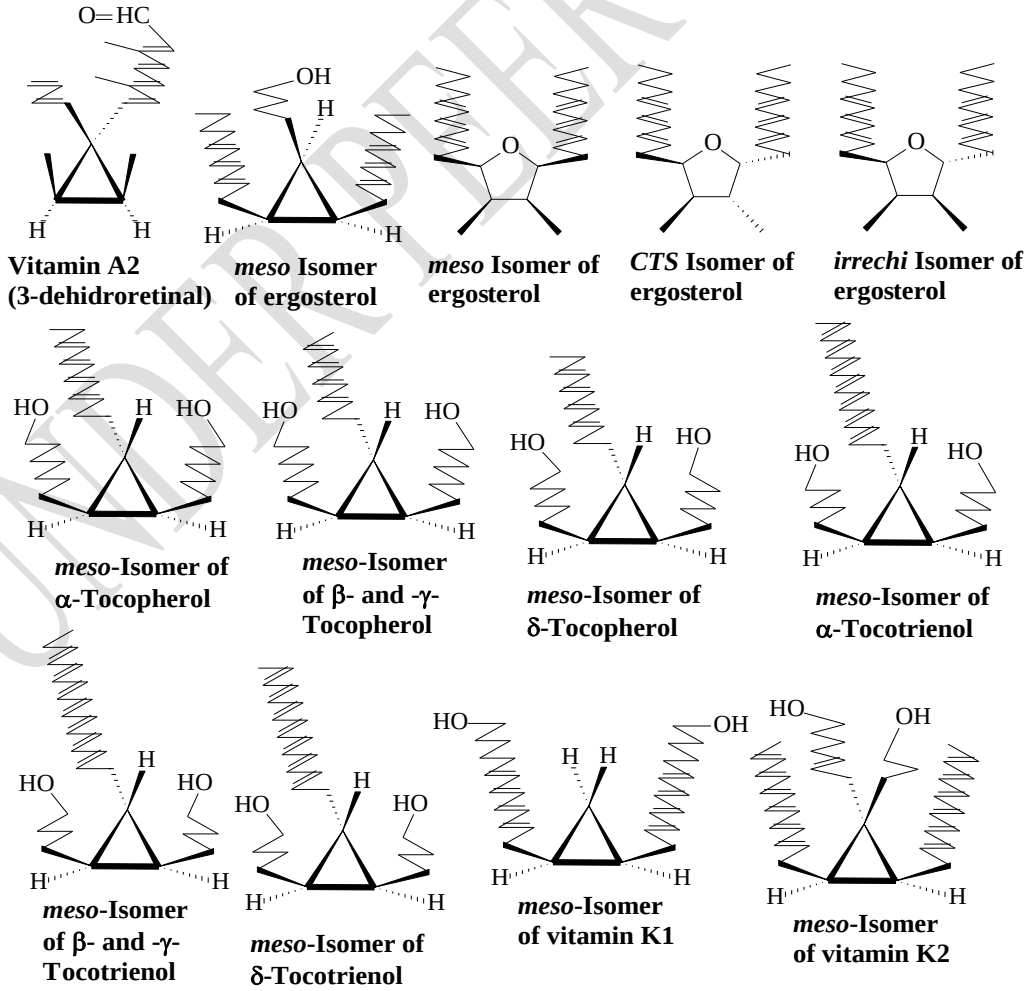

Figure 10.*Meso* isomers of lipophilic vitamins.

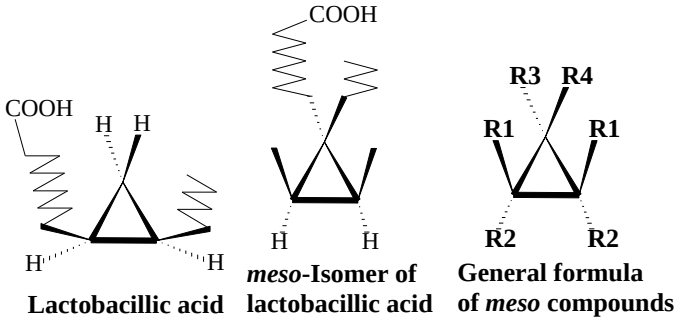

Figure 11. Source of inspiration and the sense of mathematical equation.

y, z, w are suitably selected numbers. x, y, z, w are connected with R1, R2, R3, R4, respectively. The rings of three or four atoms, as cycles or heterocycles, synthetic [14,97-99] or found in natural materials, are well known. Cis- and trans-1,2-dimethyl cyclopropane are indistinguishable of thermodynamic point of view [100]. 1,2,3-Trihydroxycyclopropane is known as an unstable combination [101,102], however no attempt was made to stabilize it. 1,2-Dihydroxycyclopropane has been prepared by a reduction reaction of a diketone derivatives [103]. Cis-1,2-dihydroxycyclopropane has been discovered in natural material as a glycoside of α-D-galactopyranose [104] as well as in the constition of mycolic acids [105] and lactobacillic acid [85]. Oxirane ring has been identified as (3*S*)-2,3-oxidosqualene in sterols biosynthesis. Two syntheses of cis-1,2,3,4-tetrahydroxy cyclobutane have been reported [106]. Lactobacillic acid can be considered as a model for our paper (Fig. 11).

4. AN EXERCISE OF COMPARATIVE CHEMISTRY GIVES AN ANSWER TO AN UNANSWERED QUESTION – WHY IS NATURAL CHEMISTRY AS IT IS ?

A question should be raised concerning the hierarchy [47] of the four types of isomers, in other words which of them fills the top place. An intrinsic property of *meso* combinations is their character of dimerism, hence their molecule is formed of two entities that are contrary in a spatial and optical sense. Of this reason, nine philosophers of ten, probably, should declare *meso* group as being on the top. We ourselves have selected them as structural reference since we thought they have a higher rank than *CTS* and *irrechi*. In fact, *meso* phenomenon is a distinct and profound philosophical category, totaly unexploited by this all-embracing science. Nonetheless, that some people could be fascinated by *CTS* molecules, since they are produced by doubling of the same entity. If we compare the four types, it's quite obvious that *meso*, *CTS* and even *irrechi* are characterized by some structural restrictions. *Constit*., molecules are characterized by fewer such structural restrictions. Of this reason, probably, natural chemistry opted for them.

When physical chemistry appeared and grew stronger, biologists and other scholars connected with biochemistry, optimistically entertained the hope that physical chemists would discover a marker for natural compounds, as density is for gold. Till now such hope never met, according to our knowledge. Nonetheless, natural combinations possess some unique characteristics, and one of them, in our opinion, is the fact that they are less restricted, in structural sense, than *meso*, *CTS* and *irrechi*. A proof for this assertion is the fact that as soon as a living thing dies, nature sends a thousand messengers to recover its component materials. We reckon that at least one of these characteristics is that *constit*. compounds have a higher number of freedom degrees, in comparison with the other types. Somehow, this phenomenon is a chemical expression of freedom.

In different classes of compounds which constitute series, a limit has been noticed, and above this limit at least *meso* isomers are possible, or even all four types. Compounds under this limit

have to be considered as archaic. They can reach to the group of combinations able of producing *meso* isomers only by chemical transformations. E. g. propane belongs to archaic group, however, by oxidation it becomes propanoic acid, an advanced form able to present *meso* form. Fischer [17,73] illustrated this by preparing a variety C_6 monosaccharides from formaldehyde or C_3 derivatives.

CONCLUSIONS

1. Atoms or fragmens cut by the mirror plane of symmetry are masked (hidden) of polarized light, and what remains, as evidenced by this physical instrument, is a homodimer.
2. All major natural metabolites possessing a significant alkane moiety and a minimum degree of oxidation have a *meso* isomer, hence a dimeric matching.
3. Of the four types of isomers – *meso*, *C_2 symmetrical*, *irrechi*, *constitutional* – nature selected *constitutional* ones, since they are characterized by the highest number of freedom degrees.
4. A triunghiular symbol can be imagined, able to represent numerous natural and synthetic compounds, providing the afore mentioned conditions are met.
5. *Meso* phenomenon discloses a new facet of natural compounds.

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