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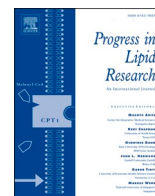
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## Review Article

An update of isoprostanoid nomenclature<sup>☆</sup>Camille Oger<sup>a,\*</sup>, Tereza Pavlíčková<sup>a,b</sup>, Valérie Bultel-Poncé<sup>a</sup>, Alexandre Guy<sup>a</sup>, Jean-Marie Galano<sup>a</sup>, Ullrich Jahn<sup>b,\*</sup>, Thierry Durand<sup>a</sup><sup>a</sup> Pôle Chimie Balard Recherche, Institut des Biomolécules Max Mousseron, IBMM UMR 5247, Univ. Montpellier, CNRS, ENSCM, 1919 route de Mende, 34293 Montpellier, Cedex 5, France<sup>b</sup> Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences, Flemingovo nám. 2, 166 10, Prague 6, Czech Republic

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## ABSTRACT

Polyunsaturated fatty acids (PUFAs) play numerous roles in living organisms but are also prone to rapid aerobic oxidation, resulting in the production of a wide range of isomeric metabolites called oxylipins. Among these, isoprostanes, discovered in the 1990s, are formed non-enzymatically from  $\omega$ -3 and  $\omega$ -6 PUFAs with 16 to 22 carbon atoms. Over nearly 35 years of research, two nomenclature systems for isoprostanes have been proposed and have evolved. However, as research progresses, certain aspects of the current nomenclature remain unclear and require further clarification to ensure precise identification of each metabolite and its corresponding parent PUFA. Therefore, we propose an update to the current nomenclature system, along with practical guidelines for assessing isoprostanoid diversity and identifying their PUFA origins.

## 1. Introduction

Thirty years ago, Jason D. Morrow and his team discovered prostaglandin (PG)-like structures produced from arachidonic acid (AA, C20:4  $\omega$ -6) through a cyclooxygenase-independent mechanism. These compounds, named isoprostanes, are isomeric to prostaglandins but feature *cis*-configured side chains instead of the *trans*-configuration found in PGs (Scheme 1). [1] Following this discovery, analogous oxygenated metabolites were identified from other polyunsaturated fatty acids (PUFAs) besides AA, and grouped under the term isoprostanoids. For example  $\alpha$ -linolenic acid (ALA, C18:3  $\omega$ -3), [2] docosahexaenoic acid (DHA, C22:6  $\omega$ -3), [3] eicosapentaenoic acid (EPA, C20:5  $\omega$ -3), [4] and adrenic acid (AdA, C22:4  $\omega$ -6) are leading to the formation of phytoprostanes, neuroprostanes, isoprostanes and dihom-isoprostanes, respectively. [5] These isoprostanoids exhibit the same diversity of ring substitution patterns as PGs, including the formation of hydroxy ketones. [6]

These discoveries necessitated the development of nomenclature systems to distinguish these PUFA metabolites from PGs. In the same year, Joshua Rokach and Douglass F. Taber proposed two nomenclature systems; [7,8] Rokach's system relied on the PG nomenclature, while Taber's followed the International Union of Pure and Applied Chemistry (IUPAC) rules. Both nomenclature systems were used in parallel, though the use of Rokach's system has declined over time.

Over the following years, extensive research has been conducted in this expanding field, leading to the discovery of new PUFAs and metabolites. [5,9] This progress has also introduced inconsistencies in the nomenclature. In particular, non-chemists often struggle with the chemical terminology used in these naming conventions.

For these reasons, we concentrated our efforts in this article on the nomenclature system proposed by Douglass F. Taber, which follows the IUPAC rules. We propose modifications to make this system more convenient and we include tips and tricks for predicting structures of isoprostanoid metabolites from a parent PUFA (see the Supporting

**Abbreviations:** AA, arachidonic acid; AdA, adrenic acid; ALA,  $\alpha$ -linolenic acid; COX, cyclooxygenase; DGLA, dihom- $\gamma$ -linolenic acid; DHA, docosahexaenoic acid; dihom-IsoG, dihom-isoglandin; dihom-IsoP, dihom-isoprostane; dihom-PhytoG, dihom-phytoglandin; dihom-PhytoP, dihom-phytoprostane; dinor-PhytoG, dinor-phytoglandin; dinor-PhytoP, dino-phytoprostane; DPA, docosapentaenoic acid; EPA, eicosapentaenoic acid; ETA, eicosatetraenoic acid; ETE, eicosatrienoic acid; GLA,  $\gamma$ -linolenic acid; HTTA, hexadecatetraenoic acid; IsoG, isoglandin; IsoP, isoprostane; IUPAC, International Union of Pure and Applied Chemistry; NeuroG, neuroglandin; NeuroP, neuroprostane; OPA, octadecapentaenoic acid; PG, prostaglandin; PhytoG, phytoglandin; PhytoP, phytoprostane; PUFA, polyunsaturated fatty acid; SDA, stearidonic acid.

<sup>☆</sup> In memory of Jason D. Morrow and Jackson Roberts II for their pioneering work in the field of isoprostanes.

\* Corresponding author.

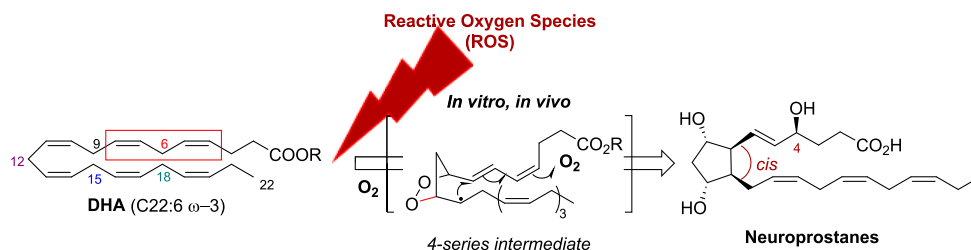
E-mail address: [camille.oger@umontpellier.fr](mailto:camille.oger@umontpellier.fr) (C. Oger).

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**Scheme 1.** Schematic representation of non-enzymatic PUFA metabolism exemplified for docosahexaenoic acid (DHA)

Information).

## 2. Polyunsaturated fatty acids and isoprostanoid biosynthesis

Polyunsaturated fatty acids (PUFAs) are fatty acids that contain more than one double bond. However, a minimum of three double bonds is required to form isoprostanoids. Table 1 summarizes all PUFAs that are expected to produce isoprostanoids, ranging from C16 to C22 in carbon length and containing three to six double bonds.

## 3. Biosynthesis of isoprostanoids and main differences with PGs

The biosynthesis of isoprostanoids is well documented. [10–13] For better context regarding the discussion points in this article, the biosynthesis of isoprostanoids is briefly outlined in Scheme 2. The process begins with the abstraction of a hydrogen atom at bis-allylic positions of the membrane-bound PUFA (in this case, DHA esters) by free radicals, such as  $\text{OH}^\bullet$ . This forms a delocalized pentadienyl radical **B1**, which then reacts with molecular oxygen to generate a peroxy radical **B2**. An initial 5-*exo*-cyclization produces an endoperoxide **B3** adjacent to a C-radical that undergoes a second 5-*exo*-cyclization, forming a cyclopentane ring with two side chains: the  $\alpha$ -chain with the carboxylic acid function and the  $\omega$ -chain (highlighted in colored boxes). The resulting delocalized allyl radical on the chain subsequently reacts with another oxygen molecule, and the peroxy radical formed abstracts a hydrogen atom to produce the hydroperoxide of the G-Neuroprostanes (G-NeuroPs **B4**). Importantly, the 5-*exo*-cyclization can yield four diastereoisomers through four transition states. However, according to the Beckwith-Houk rules, cyclization predominantly results in a relative *cis*-configuration of the chains. At this stage, phospholipase A2 (PLA<sub>2</sub>) cleaves the hydroperoxides, linked to the membrane as phospholipids or glycolipids, and further reduction of the hydroperoxides occurs, leading to the formation of the allylic alcohol function in H-isoprostanoids **B5**.

H-isoprostanoids serve as advanced intermediates for the isoprostanoids. The reduction or rearrangement of H-isoprostanoids results in various oxygen functionalizations at the 5-membered ring (Scheme 3). Specifically, complete reduction of the endoperoxides produces F-type isoprostanoids, characterized by a *cis*-1,3-diol on the cyclopentane ring. A Kornblum-DeLaMare rearrangement of the H-isoprostanoids generates the D- and E-type hydroxy ketone substitution patterns. Further dehydration of the D- and E-types leads to the formation of J- and A-type isoprostanoids, respectively, each featuring  $\alpha,\beta$ -unsaturated ketone units. Note that in plants, B- and L-types, where the  $\alpha,\beta$ -unsaturated ketone function is located at the carbon atoms bearing the side chains, were also discovered. [14]

Isoprostanoids are formed as racemic mixtures, with several possible regioisomers depending on the regioselectivity of the initial hydrogen abstraction and subsequent reactions with oxygen. Scheme 2 shows abstraction at the C6 carbon atom, but it can also occur at other bis-allylic positions (C9, C12, C15, C18). The radical pathway in isoprostanoid biosynthesis primarily produces *cis*-configured isoprostanoids. However, *trans*-configured isoprostanoids, though minor metabolites, can also be formed. Currently, the major *trans*-configured PUFA metabolites are PGs, which are produced *in vivo* from non-

esterified PUFAs within the active site of cyclooxygenase (COX). The COX active site facilitates the formation of PGs as a single stereoisomer with a defined absolute configuration (Fig. 1, PGF<sub>2 $\alpha$</sub> ).

It is worth noting that the primary PGs are derived from AA, which is the main PUFA substrate for COX. Other non-esterified acid PUFAs have also been identified as COX substrates *in vitro*, through the formation of monohydroxylated fatty acids, including ALA,  $\gamma$ -linolenic acid (GLA), dihomo- $\gamma$ -linolenic acid (DGLA), EPA, and AdA. [15–17] However, the efficiency of these substrates for human COX decreases in the order of AA > DGLA > AdA > ALA > EPA. This hierarchy needs confirmation *in vivo*.

Considering the structural diversity and stereochemistry of isoprostanoids, which are chemically similar to PGs but originate from different biosynthetic pathways, it is crucial to propose a nomenclature that allows both specialists and non-specialists to navigate the field easily.

## 4. Current nomenclature

All isoprostanoids share common structural features resulting from biosynthesis, including a cyclopentane ring and two lateral chains with one or several double bonds, along with a hydroxyl function (as illustrated in Fig. 2). The  $\alpha$ -chain, which bears the carboxylic acid function, is typically depicted at the top of the structure. Despite these commonalities, individual isoprostanoid structures vary in the total number of carbon atoms, the position and number of double bonds, and, as previously mentioned, the relative position of the two chains and the extent of oxygenation of the cyclopentane ring. Hence, to uniformly identify each structure, a nomenclature system was necessary. Out of the two nomenclature systems proposed originally, [7,8] only the one described and amended by Douglass F. Taber is detailed here (Fig. 2).

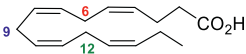
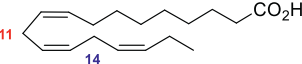
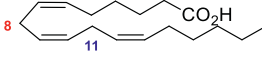
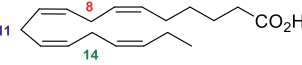
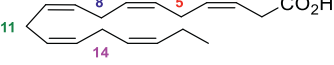
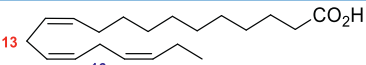
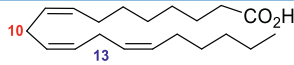
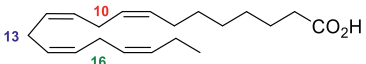
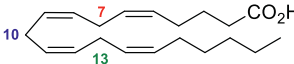
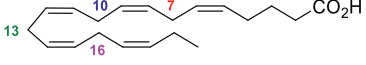
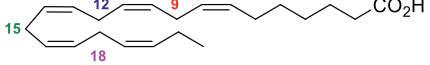
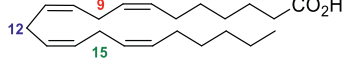

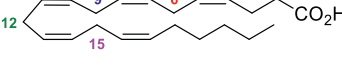
To assign an isoprostanoid name, and to propose a nomenclature as clearly as possible, default configurations were established as follows (Fig. 3).

First, inherent to the biosynthesis, in consideration of the formation of major metabolites only, the two side chains have *cis*-configuration. Second, the two hydroxy groups of the F-type cyclopentane diol always have a *cis*-configuration, and they are by default depicted by  $\alpha$ -configuration (or (*S*<sup>\*</sup>)) by analogy to PGs. Similarly, the default relative configuration of the side chain allylic hydroxy group is (*S*<sup>\*</sup>).

This pattern of rules is then followed (from left to right) [7]:

1. Assign the position of the side chain allylic hydroxyl group by a number (in green, Fig. 2). Numbering of isoprostanoids' skeleton assigns number C-1 to the carboxyl group and continues along the chain.
2. Add a prefix describing the ring substitution pattern by a capital letter as F-, E-, D-, A-, J-, B- or L- (for all patterns see Scheme 3).
3. Add a subscript to the ring-substitution letter marking the number of double bonds on the side chains of the molecule (in red, Fig. 2).
4. Add the first stereodescriptor to assign the relative configuration of the hydroxy group(s) with respect to the chain follows with various degree of oxygenation the number of double bonds: t for *trans* (as in compounds I and II) and c for *cis* (as in compound IV).

**Table 1**  
Summary of PUFAs (C16 to C22) and their structures.

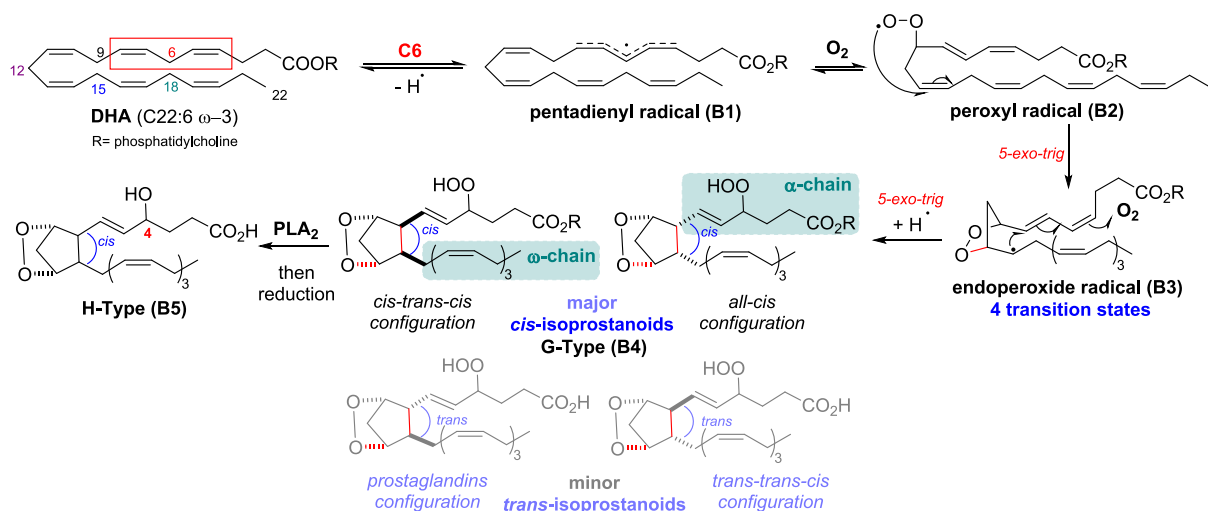
$\omega-3$		$\omega-6$
<b>C16</b>		
 <p><b>HTTA (C16:4 <math>\omega-3</math>)</b> <b>Hexadecatetraenoic acid</b></p>		
<b>C18</b>		
 <p><b>ALA (C18:3 <math>\omega-3</math>)</b> <b>α-linolenic acid</b></p>		 <p><b>GLA (C18:3 <math>\omega-6</math>)</b> <b>γ-linolenic acid</b></p>
 <p><b>SDA (C18:4 <math>\omega-3</math>)</b> <b>stearidonic acid</b></p>		
 <p><b>OPA (C18:5 <math>\omega-3</math>)</b> <b>octadecapentaenoic acid</b></p>		
<b>C20</b>		
 <p><b>ETE (C20:3 <math>\omega-3</math>)</b> <b>eicosatrienoic acid</b></p>		 <p><b>DGLA (C20:3 <math>\omega-6</math>)</b> <b>dihomo-γ-linolenic acid</b></p>
 <p><b>ETA (C20:4 <math>\omega-3</math>)</b> <b>eicosatetraenoic acid</b></p>		 <p><b>AA (C20:4 <math>\omega-6</math>)</b> <b>arachidonic acid</b></p>
 <p><b>EPA (C20:5 <math>\omega-3</math>)</b> <b>eicosapentaenoic acid</b></p>		
<b>C22</b>		
 <p><b>DPA (C22:5 <math>\omega-3</math>)</b> <b>docosapentaenoic acid</b></p>		 <p><b>AdA (C22:4 <math>\omega-6</math>)</b> <b>adrenic acid</b></p>
 <p><b>DHA (C22:6 <math>\omega-3</math>)</b> <b>docosahexaenoic acid</b></p>		 <p><b>DPA (C22:5 <math>\omega-6</math>)</b> <b>docosapentaenoic acid</b></p>

5. Assign the type of metabolite as PhytoP (phytoprostane), IsoP (isoprostane) or NeuroP (neuroprostane).

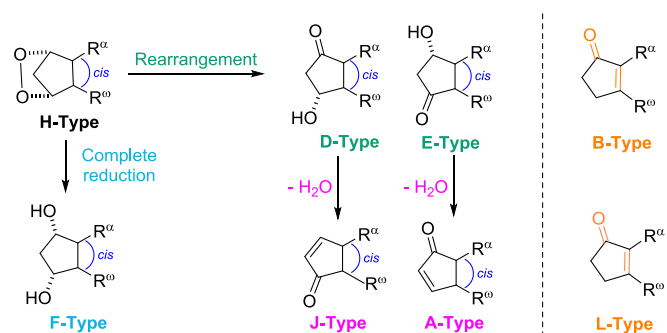
Note that at the time of the original proposal, three types of isoprostanoids had been identified: isoprostanes (IsoPs) from AA, phytoprostanes (PhytoPs) from ALA and neuroprostanes (NeuroPs) from DHA.

It was later generally accepted that the 18-carbon isoprostanoids would be called PhytoPs, C20 named IsoPs and C22 carbon atoms called NeuroPs (see Fig. 2).

6. If needed, complete the nomenclature by adding every deviation from the default configuration by prefixes. One or two such



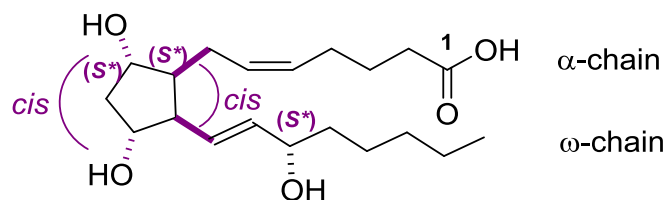
**Scheme 2.** First steps in the biosynthesis of isoprostanoids as exemplified for the conversion of DHA to 4-H<sub>4</sub>-neuroprostane (4-NeuroP)



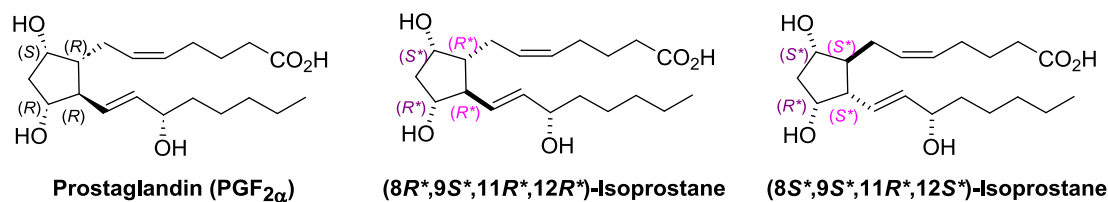
**Scheme 3.** Final steps in the biosynthesis of isoprostanoids leading to the diversity of functionalization of the 5-membered ring

deviations (e.g., hydroxyl group or α-chain) are described by a prefix *epi-* or *diepi-* preceded by the corresponding carbon number (as in compounds II and III).

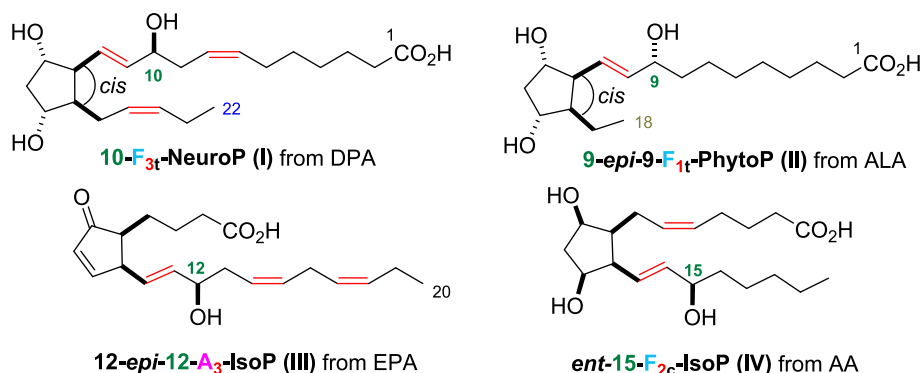
If more than two stereocenters differ from the default configuration, or if the ring hydroxy groups have β-configuration, the prefix *ent-* for “enantiomer” should be used followed by other prefixes, if necessary (compound IV, Fig. 2). Note that the default configuration of an *ent-*



**Fig. 3.** Default configurations for naming isoprostanoids.



**Fig. 1.** Prostaglandins versus isoprostanoids (from AA).



**Fig. 2.** Examples of isoprostanoid nomenclatures (current nomenclature).

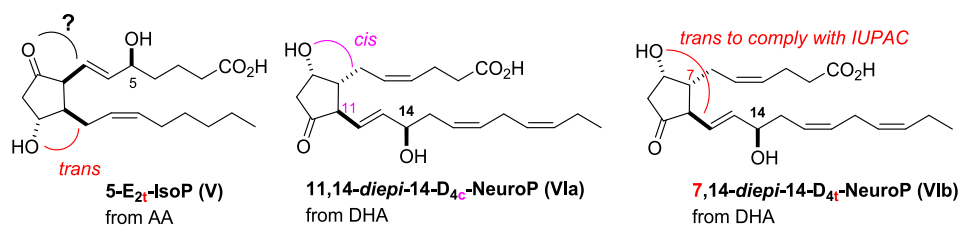


Fig. 4. Examples of limitation of the current nomenclature.

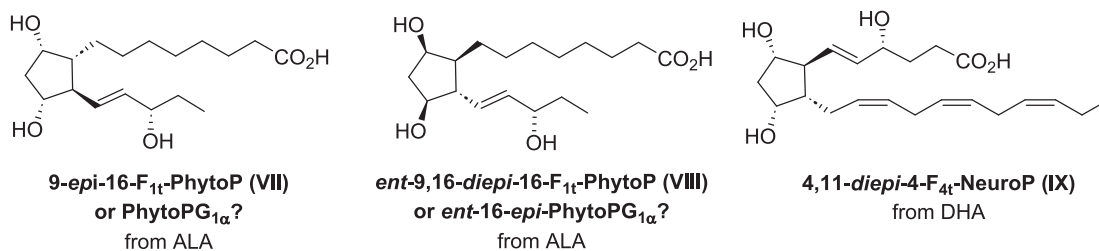


Fig. 5. Prostaglandin-like compounds synthesized by Jahn's and Durand's groups.

compound is the opposite at all stereocenters including the side chain hydroxyl group, which should thus be (*R*\*). Also, note that for A- and J-types, no hydroxyl groups can be used to describe the relative configuration as *cis* or *trans* (as in compound III, Fig. 2).

## 5. Current nomenclature limitations

Despite its straightforwardness and ease of use, the current nomenclature system faces significant limitations due to the increasing number of these metabolites and the discovery of numerous new PUFAs. One major issue is the lack of clear specification regarding which side chain or hydroxy group should be considered when assigning *cis* or *trans* configurations. The common interpretation involves assessing the relative configuration between the  $\alpha$ -chain and the adjacent ring hydroxy group. However, this poses challenges when naming E-type structures, as there is no hydroxy group next to the  $\alpha$ -chain (as seen in compound V, Fig. 4).

Moreover, following this interpretation, compound VI could be named 11,14-*diepi*-14- $D_{4c}$ -NeuroP (as in compound VIa). However, this naming convention does not adhere to IUPAC rules, which dictate that the prefix “*epi*” should be assigned to the carbon with the lowest numbering. Following this rule, the  $\omega$ -chain should be taken as a reference instead of the  $\alpha$ -chain to assign the *trans* configuration, resulting in an alternative name, 7,14-*diepi*-14- $D_{4t}$ -NeuroP, for the same compound (VIb).

Furthermore, as demonstrated by Yin et al. [13] for AA, and illustrated in Scheme 2, the radical 5-*exo*-cyclization for accessing the cyclopentane ring is not stereoselective. While it primarily proceeds via a Beckwith-Houk transition state, resulting in relative *cis*-configurations of the side chains, *trans*-configured isoprostanoids, resembling prostaglandin-like structures, are also formed. Additionally, epimerization at the  $\alpha$ -position to the ketone group of E-, D-, A-, or J-type

isoprostanoids, which occurs even at physiological pH, [18] may lead to *trans* configurations of the side chains, even that they may have been originally *cis*. In this context, recent work by Jahn's and Durand's groups has described syntheses of isoprostanoids with *trans* configurations (Fig. 5). [19,20]

Importantly, the presence of *trans*-PhytoPs (compounds VII and VIII) has been highlighted *in vivo* in plant-based foodstuffs, indicating their origin from the autoxidation of  $\alpha$ -linolenic acid. Thus, it would be advantageous for the nomenclature system to allow for quick determination of the relative configuration of side chains.

Since the inception of the original nomenclature, the increasing interest in these metabolites has spurred numerous studies on various PUFAs, leading to the discovery of new isoprostanoids. As mentioned earlier, it was widely accepted that isoprostanoids with 18, 20, and 22 carbon atoms would be termed PhytoPs, IsoPs, and NeuroPs, respectively. However, when Van Rollins et al. [5] discovered cyclic adrenic acid (AdA, C22:4  $\omega$ -6) metabolites such as XI, they opted to name them in analogy to IsoPs X with a prefix “*dihomo*-” because AdA possesses two additional carbon atoms compared to AA (C20:4  $\omega$ -6) (Fig. 6). Although this prefix is still used to maintain consistency with their discovery and subsequent work, it has not been explicitly stated in the current nomenclature.

Another ambiguity arises when two PUFAs with the same number of carbon atoms and double bonds differ from each other by having  $\omega$ -6 or  $\omega$ -3 chains, as illustrated by docosapentaenoic acids  $DPA_{\omega-6}$  and  $DPA_{\omega-3}$ , respectively. Their autoxidative cyclizations lead to the formation of metabolites I and XII, respectively (Fig. 7). However, the current nomenclature system would assign the same name, 10- $F_{3t}$ -NeuroP, to both of them.

As many PUFAs are structurally very similar, and the resulting cyclic metabolites also appear similar, it can be challenging for non-specialists to determine from which PUFA a given isoprostanoid metabolite

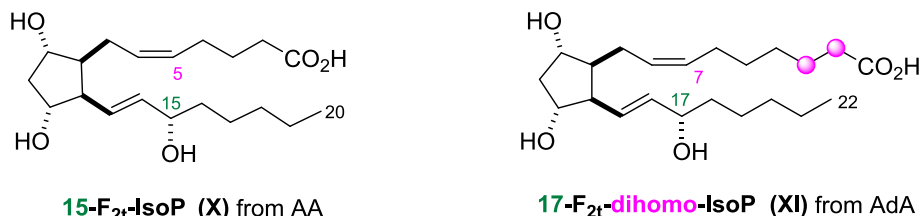


Fig. 6. Dihomo-isoprostanones and their relation to the structure of AA-derived IsoP.

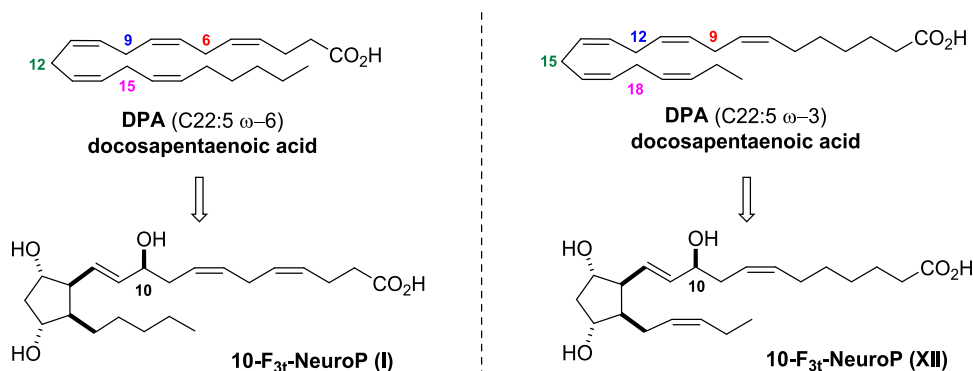


Fig. 7. An example of ambiguous isoprostanoid nomenclature.

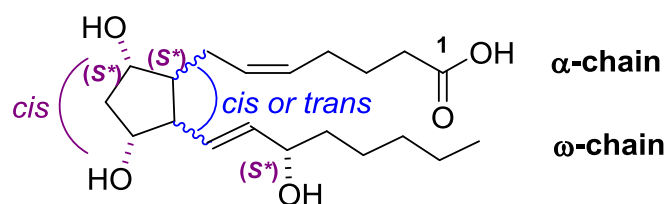


Fig. 8. Default configurations.

originates. Considering the diversity and growing interest in the field of PUFA metabolites, a unified system of nomenclature covering both *cis* and *trans* isoprostanoids is proposed herein. This system aims to address the apparent limitations and uncertainties, providing an unambiguous and expandable guide for scientists working in this field.

### 6. A unified nomenclature for *cis*- and *trans*-isoprostanoids

To answer the various questions raised above, a new nomenclature system is proposed, and the rules to assign *cis*- or *trans*-isoprostanoid

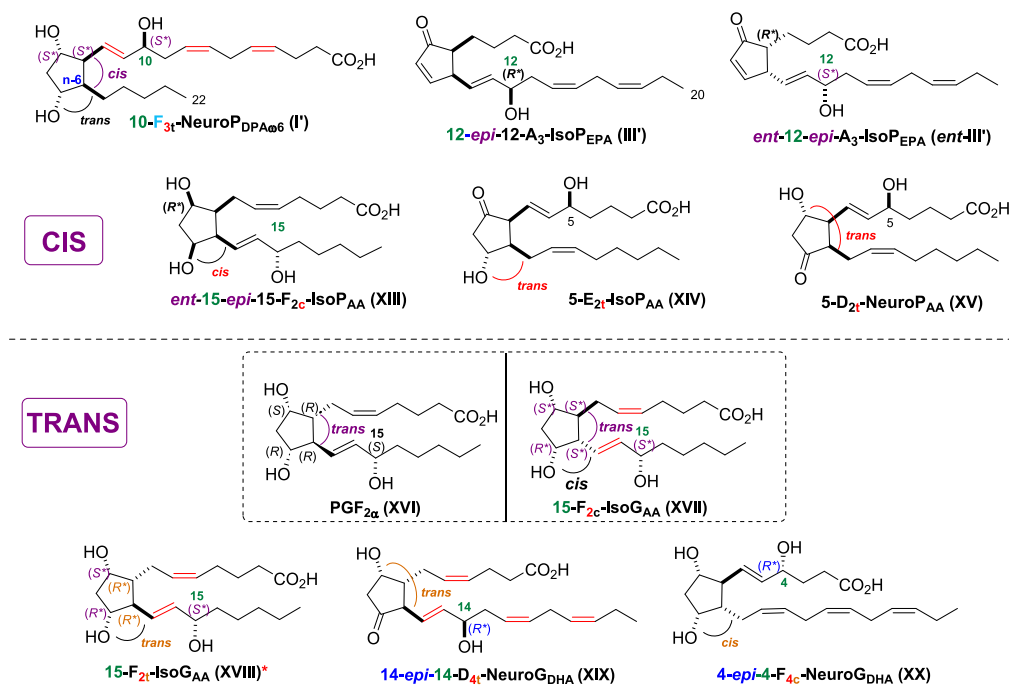


Fig. 9. Examples of isoprostanoid nomenclature. \* Note that this compound represents the racemic analog of PGF<sub>2α</sub> (XVI).

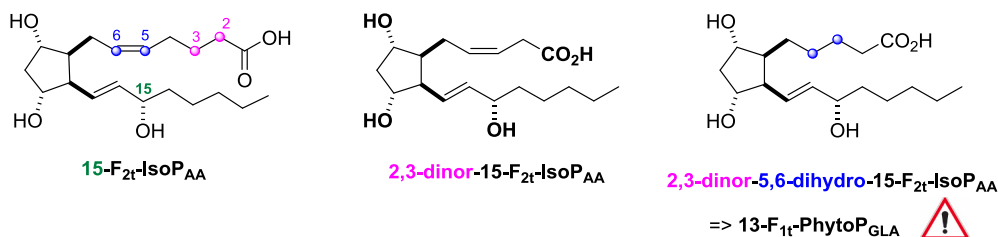


Fig. 10. 15-F<sub>2t</sub>-IsoP<sub>AA</sub> urinary metabolites.



**Table 2**

Names and abbreviations of the isoprostanoids.

Parent PUFA (abbreviations and main food sources [21]) <sup>a</sup>	<i>cis</i> -Isoprostanoid prefix before “-prostanes (P)”	<i>trans</i> -Isoprostanoid prefix before “-glandins (G)”
Hexadecatetraenoic acid (HTTA, C16:4 ω-3, fishes, algae)	<b>dinor-Phyto-</b> (dinor-PhytoP <sub>HTTA</sub> ) <sup>b</sup>	<b>dinor-Phyto-</b> (dinor-PhytoG <sub>HTTA</sub> )
α-Linolenic acid (ALA, C18:3 ω-3, plants, algae)	<b>Phyto-</b> (PhytoP <sub>ALA</sub> )	<b>Phyto-</b> (PhytoG <sub>ALA</sub> )
Stearidonic acid (SDA, C18:4 ω-3, plants, algae)	<b>Phyto-</b> (PhytoP <sub>SDA</sub> )	<b>Phyto-</b> (PhytoG <sub>SDA</sub> )
Octadecapentaenoic acid (OPA, C18:5 ω-3, algae, fishes)	<b>Phyto-</b> (PhytoP <sub>OPA</sub> )	<b>Phyto-</b> (PhytoG <sub>OPA</sub> )
γ-Linolenic acid (GLA, C18:3 ω-6)	<b>Phyto-</b> (PhytoP <sub>GLA</sub> )	<b>Phyto-</b> (PhytoG <sub>GLA</sub> )
Dihomo-γ-Linolenic acid (DGLA, C20:3 ω-6, plants, corals)	<b>dihomo-Phyto-</b> (dihomo-PhytoP <sub>DGLA</sub> )	<b>dihomo-Phyto-</b> (dihomo-PhytoG <sub>DGLA</sub> ) <sup>c</sup>
Arachidonic acid (AA, C20:4 ω-6, eggs, meat, algae)	<b>Iso-</b> (IsoP <sub>AA</sub> )	<b>Iso-</b> (IsoG <sub>AA</sub> )
Eicosapentaenoic acid (EPA, C20:5 ω-3, fishes, algae)	<b>Iso-</b> (IsoP <sub>EPA</sub> )	<b>Iso-</b> (IsoG <sub>EPA</sub> )
Adrenic acid (AdA, C22:4 ω-6, algae)	<b>dihomo-Iso-</b> (dihomo-IsoP <sub>AdA</sub> )	<b>dihomo-Iso-</b> (dihomo-IsoG <sub>AdA</sub> )
Docosapentaenoic acid (DPA, C22:5 ω-6, fishes)	<b>Neuro-</b> (NeuroP <sub>DPAω-6</sub> )	<b>Neuro-</b> (NeuroG <sub>DPAω-6</sub> )
Docosapentaenoic acid DPA (C22:5 ω-3, fishes, seal meat)	<b>Neuroprostanes</b> (NeuroP <sub>DPAω-3</sub> )	<b>Neuroglandins</b> (NeuroG <sub>DPAω-3</sub> )
Docosahexaenoic acid (DHA, C22:6 ω-3, fishes, algae)	<b>Neuroprostanes</b> (NeuroP <sub>DHA</sub> )	<b>Neuroglandins</b> (NeuroG <sub>DHA</sub> )

<sup>a</sup> It should be mentioned that from α-linolenic acid thanks to elongase and desaturase enzymes organisms are able to synthesized C22-PUFA, see references [22,23] for the global biosynthetic pathway.

<sup>b</sup> So far, not known.

<sup>c</sup> It should be mentioned that enzymatically formed PGF<sub>1α</sub> is identical to the dihom-PhytoG structure derived from DGLA.

names are described herein (Fig. 9). Note that rules 1.-3. and 5. remain the same as above.

1. Assign the position of the side chain allylic hydroxyl group by a number (in green, Fig. 2). Numbering of isoprostanoids' skeleton assigns number C-1 to the carboxyl group and continues along the chain.
2. Add a prefix describing the ring substitution pattern by a capital letter as F-, E-, D-, A-, J-, B- or L- (for all patterns see Scheme 3).
3. Add a subscript to the ring-substitution letter marking the number of double bonds on the side chains of the molecule (in red, Fig. 2).
4. Add the first stereodescriptor to assign the relative configuration of the hydroxy group(s) with respect to the ω-chain. The descriptors remain the same: t for *trans* and c for *cis*.

Note that the default configurations (Fig. 8) remain the same, except for the relative configuration of the side chains, that can now be *cis* or *trans*.

5. Assign the type of metabolite as PhytoP (phytoprostane), IsoP (isoprostane) or NeuroP (neuroprostane).
6. Add a suffix that would give information either on the number of carbons, and/or on the origin of the parent PUFA.

According to previous nomenclature: “**Phyto-**” for the PUFA found in plants, seeds, algae, and other marine organisms, “**Iso-**” for the main C20-PUFAs (AA and EPA), and “**Neuro-**” for the main C22-PUFA. Also, “**dihomo-**” prefix is kept for the AdA derived metabolites, and thus added for dihom-γ-linolenic acid (DGLA)

metabolites, referring to the two additional carbon atoms from γ-linolenic acid (GLA). On the other hand, prefix “**dinor**” will be used for the metabolites with 16 carbon atoms (see chapter VII for more details).

7. Complete the nomenclature by a suffix referring to the type of metabolite: “**-prostanes (P)**” and “**-glandins (G)**” for *cis*- and *trans*-isoprostanoids respectively.
8. Finally, add in subscript the abbreviation of the parent PUFA. This will give rapid information on the parent PUFA and avoid the same name for different structures (see Table 2).

## 7. Other considerations: Isoprostanoid catabolism

Further oxidation processes may occur at the isoprostanoid skeleton, including β-oxidation, which is well-described for fatty acids. This catabolic process involves a four-step enzymatic sequence utilizing reductase, dehydrogenase, and hydratase enzymes, ultimately resulting in the removal of two carbon atoms, as shown in Scheme 4. In chemical nomenclature, the prefix “nor” is used to denote a structural analog of a compound resulting from the removal of one carbon atom. Consequently, β-oxidation of isoprostanoids yields “dinor-, tetranor-, hexanor-” metabolites.

Additionally, during β-oxidation, intermediates such as hydrogenated compounds or ketones may be formed and found *in vivo*. In such cases, the prefixes “hydro-” or “keto-” are used respectively.

Awareness of the β-oxidation catabolic process is crucial, as it influences the structures of the secondary metabolites obtained, which may also serve as primary metabolites of other PUFAs. [24] For instance, 15-F<sub>2t</sub>-IsoP<sub>AA</sub> is metabolized into two new metabolites: 2,3-dinor-15-F<sub>2t</sub>-IsoP<sub>AA</sub> and 2,3-dinor-5,6-dihydro-15-F<sub>2t</sub>-IsoP<sub>AA</sub> (Fig. 10). [25,26] The structure of the latter is identical to that of 13-F<sub>1t</sub>-PhytoP<sub>GLA</sub>, a metabolite of γ-linolenic acid (GLA). Therefore, every scientist in this field should consider the context of the study performed and be mindful of the metabolization process to ensure appropriate data analysis. Practitioners can avoid confusion by correctly adhering to the newly proposed nomenclature update, from which the parent PUFA becomes apparent.

## 8. Conclusion

Isoprostanoids have emerged as valuable biomarkers of oxidative stress and exhibit pharmacological properties. While the initial nomenclature proposed after the discovery of these metabolites was effective, limitations and inaccuracies have surfaced over the years, necessitating amendments.

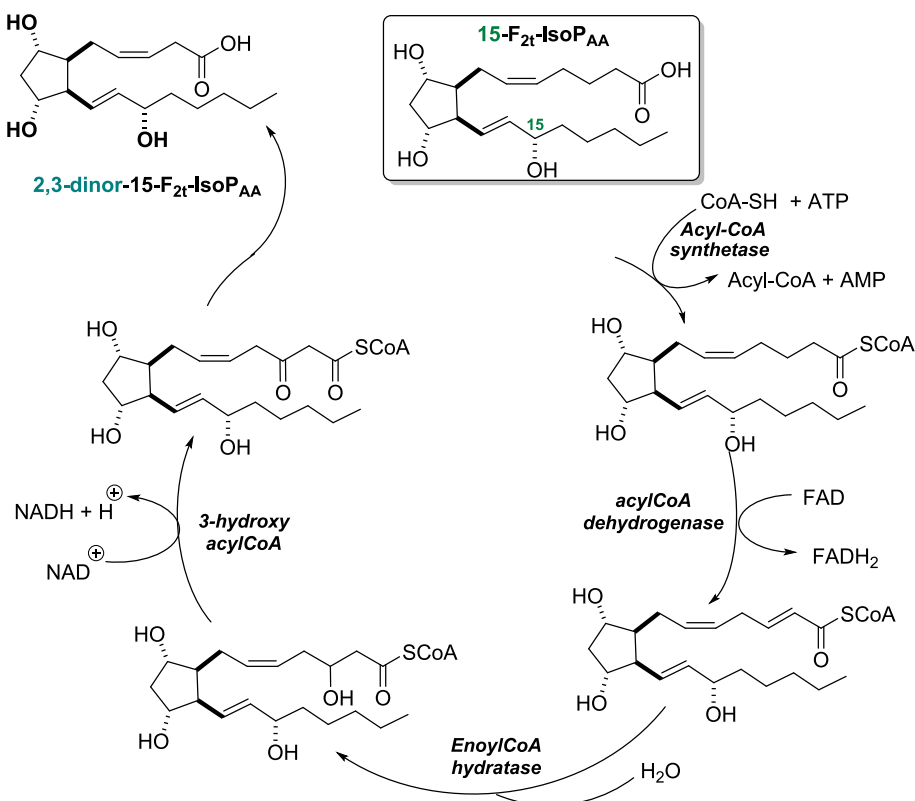
This work proposes a significant extension of the original nomenclature system for isoprostanoids with lateral chains in relative *cis*-configuration. Since the radical process of isoprostanoid formation is not stereoselective, isoprostanoids with lateral chains in *trans*-configuration are also formed and found *in vitro* and/or *in vivo*. To account for their presence and potential bioactivities, a unified nomenclature system encompassing both *cis*- and *trans*-configured isoprostanoids is proposed here.

Furthermore, as research on autoxidatively formed isoprostanoids attracts researchers from various disciplines, this work also offers tips and tricks to quickly become familiar with the structures of isoprostanoids and their relationships to the parent PUFAs.

## CRedit authorship contribution statement

**Camille Oger:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Tereza Pavlíčková:** Writing – review & editing, Writing – original draft, Conceptualization. **Valérie Bultel-Poncé:** Writing – review & editing. **Alexandre Guy:** Writing – review & editing, Conceptualization. **Jean-Marie Galano:** Writing – review & editing, Validation. **Ullrich Jahn:**





Scheme 4.  $\beta$ -oxidation of 15-F<sub>2t</sub>-IsoP<sub>AA</sub> – formation of 2,3-dinor-15-F<sub>2t</sub>-IsoP<sub>AA</sub>.

Writing – review & editing, Writing – original draft, Conceptualization.

**Thierry Durand:** Writing – review & editing, Resources.

#### Declaration of competing interest

None.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.plipres.2024.101301>.

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