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Isoprostane nomenclature: Inherent problems may cause setbacks for the development of the isoprostanoid field

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ABSTRACT

Do we have to bother about the isoprostane nomenclature? The widely accepted IUPAC isoprostane nomenclature provides an unambiguous and systematic terminology to name all theoretical possible isoprostanes. However, the currently accepted nomenclature system provides an unnatural framework which is not well suited to address certain biologically relevant questions. Artificial categorization of isoprostanoids into prostanoid families disrupts prostaglandin-ring core structures needed to describe biogenetic precursor–product relationships. In addition, the IUPAC system defines isoprostanoid families which comprise chemically heterogeneous isoprostanoids which largely differ in their physicochemical properties from those of the corresponding prostaglandins. As a result of this, alternative nomenclature systems such as the phytoprostane nomenclature system overcoming some inherent problems of the IUPAC nomenclature are still in use. However, different naming of isoprostanoids especially the classification of prostanoid family names has created considerable confusion. Therefore, a cautionary note on the current use of different nomenclature systems is necessary.

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1. Introduction

All nomenclature systems are artificial systems put into use by definition and convention. An isoprostanoid nomenclature system should permit unambiguous names for all theoretically possible isomers that can not only be formed through isoprostanoid pathways from polyunsaturated fatty acids but also chemically synthesized congeners and derivatives. Ideally, the names should intuitively relate to prostaglandins, allow convenient indexing and retrieval of information, allow easy visualization of structures and provide scientists of different disciplines with a practical, easy and systematic-rational system to name structures. At best, nomenclature systems are natural systems that provide an adequate language to address biologically relevant questions.

Currently, besides the prostaglandin nomenclature, three different nomenclature systems are used to name hundreds of different isoprostanoids. Parallel use of different nomenclatures

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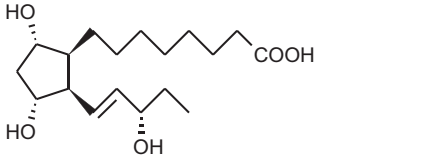
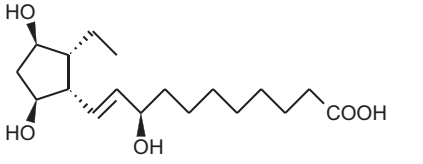
has created considerable confusion in the field. This is not only because different names are used for same compounds but more importantly because different nomenclatures differ in their classification of isoprostanoid families. For instance, the three systems proposed by Taber et al. [1], Rokach et al. [2] and Mueller [3] lead to completely different names for the same structures (Fig. 1). The principles of all nomenclature systems are briefly described before discussing merits and inherent problems of each system.

2. Prostaglandin nomenclature (1974)

The prostaglandin nomenclature proposed by Nelson in 1974 employs prostanoic acid (Fig. 2) as stereo- and indexing heading parent structure [4]. Prostaglandins have been divided into A, B, C, D, E, etc. families and differ from each other in the functionality of the five-membered ring as illustrated in the partial structures shown in Fig. 2. The structures of prostaglandins should be represented in a consistent format with the carboxy side chain extending to the upper right side and the terminal alkyl chain extending to the lower right side of the five-membered ring. The abbreviation of prostaglandins is PG followed by the letter indicating the prostaglandin family (PGA, PGB, etc.). The number of the side chain double bonds is indicated by a subscript index number behind the family letter (i.e. PGA_1 for PGA with one side chain double bond). All naturally occurring PG are derived from common precursors comprising the core substructure of PGG (Figs. 3, **6a**) which is formed from a triene unit of polyunsaturated fatty acids by the cyclooxygenase enzyme. In PGG_2 (Fig. 4, **13a**) as well as all prostaglandin families derived from PGG, the R_1 chain is always the carboxy side chain and the R_2 chain comprises the allylic alcohol and the terminal methyl group (Figs. 3, **6a**). As discussed below, the prostaglandin core structures are not only essential for receptor binding and biological activity but also largely determine the physicochemical properties and metabolic fate of the parent compounds.



a) *ent*-16-F_{1t}-PhytoP
b) dinor-iPF$_{1\alpha}$-I
c) 9(*S*),10(*S*),12(*R*),13(*R*),14(*E*),16(*S*)-PPF$_1$-I



a) 9-F_{1t}-PhytoP
b) 9-*iso*-dinor-iPF1$_\alpha$-II
c) 9(*R*),10(*E*),12(*S*),13(*S*),15(*R*),16(*R*)-PPF$_1$-II

Fig. 1. Different names for F_1-phytoprostane according to (a) the IUPAC nomenclature, (b) the Rokach nomenclature and (c) the phytoprostane nomenclature.

3. The IUPAC isoprostane nomenclature (1997)

This nomenclature systems has been proposed by Taber et al. [1] and been accepted by the Eicosanoid Nomenclature Committee, sanctioned by JCBN of IUPAC. It is widely used in the isoprostane and neuroprostane field. Non-enzymatically formed C20 prostanoids were termed isoprostanes and abbreviated with IsoP. Later, C22 prostanoids derived from docosahexanoic acid were designated as neuroprostanes (NeuroP) [5]. In an analogous way, C18 prostanoids derived from α- or γ-linolenic acid would be phytoprostanes (PhytoP). Due to the absence of an enzyme, the substituents at the five-membered ring are racemic. The family name is derived from the substitution pattern of the five-membered ring wherein the carboxy side chain is formally defined as substituent R_1 (as in the prostaglandin nomenclature system, Fig. 2). In the Taber nomenclature system, the five-membered ring is termed the prostaglandin ring system from which the family names are derived. However, the common prostaglandin core structures and not the five-membered ring system are usually termed prostaglandin ring system. In contrast to the PG nomenclature system, the letter indicating the isoprostanoid family is placed in front: i.e. A_1-isoprostane (A_1-IsoP) etc. Next, different carbon skeletons are named according to the location of the side chain hydroxy group with C-1 being the carboxy group (i.e. 5-A_1-IsoP, etc.). These formal exercises to generate family names lead in many cases, however, to the disruption of the prostaglandin core structures (the 'prostaglandin ring systems' comprising the side chain hydroxy group). The consequences of this operation are discussed

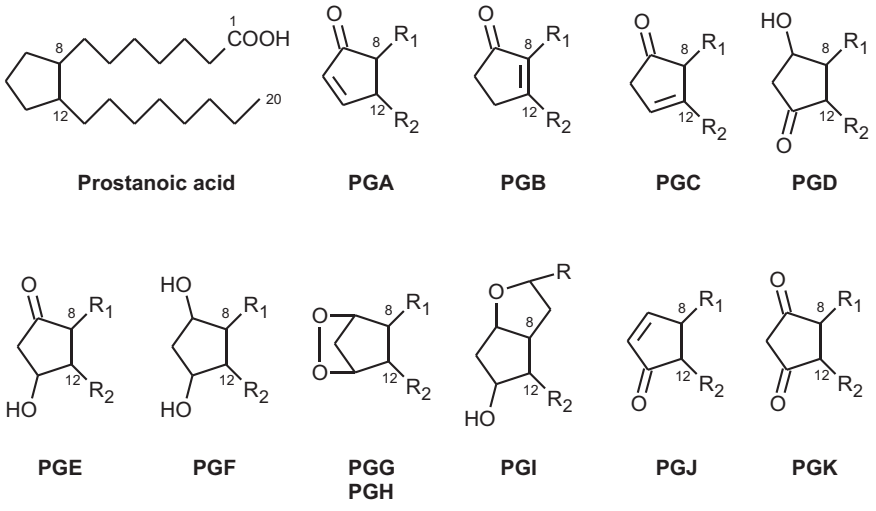


Fig. 2. Prostaglandin nomenclature. Prostanoic acid serves as index heading parent and the different prostaglandin head groups define the prostaglandin families.