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The Nomenclature of *Pandanus* Alkaloids

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Abstract

From the literature, only one percent of the total *Pandanus* species (Pandanaceae family) were analysed in the studies related to their secondary metabolites. Scientific publications offered neither a recent record of all *Pandanus* alkaloids, nor the suggestion of any classification of these biomolecules. Therefore, this paper is aimed to propose the unprecedented nomenclature of *Pandanus* alkaloids, following the inventory of their 26 natural alkaloids. From the examination, these specific compounds have a basic C_9-N-C_9 molecular framework. For an example, in the arrangement of carbon atoms of Pandanamine, the first carbon (C-1) is counted at the heteroatom of oxygen and the second carbon is attached with the ketone group. The C-1 to C-9 was assigned with one lactone skeleton. In the meantime, C-11 to C-19 showed the second lactone moiety. Furthermore, this nomenclature is determined based on its amine group. Pandanamine, being a symmetrical secondary amine, is hypothetically a biogenetic precursor of the *Pandanus* alkaloids. It has a straight chain of anime group that undergoes intramolecular cyclisation to form heterocyclic amines such as pyrrolidine (five-membered ring), piperidine (six-membered ring) and indolizidine (five- and six-membered rings). Thus, the compound that consists of piperidine alkaloid was named as pandamarilactone. Meanwhile, the molecules having pyrrolidine alkaloid was referred as pandamarilactonine. Pandanamine has two lactone rings and this might be observed in all alkaloids that were isolated from *Pandanus* species. The proposed systematic classification of the above alkaloid was utilised as well, in order to characterise two novel alkaloids, Pygmauesamine A and B, which were purified from the dichloromethane extract of *Pandanus pygmaeus*. Such compounds owning the indolizidine ring might possess biological activities such as antibacterial, fungicidal and insecticidal properties. It is anticipated that this nomenclature could be applied indefinitely, due to the relatively small number of *Pandanus'* alkaloidal structures.

Keywords: alkaloids, Pandanaceae, *Pandanus*, nomenclature, structure

Introduction

Pandanus species or the screwpines (family: Pandanaceae) are well known to contain alkaloids. To date, these alkaloids were successfully extracted from the leaves and roots of *Pandanus* plants, concentrating on *P. amaryllifolius*, *P. dubius* and *P. pygmaeus*. Other *Pandanus* are relatively less known, within approximately seven hundred documented species, compared to the famous fragrant screwpine, *P. amaryllifolius* (pandan wangi). This plant is also referred as "Vanilla of the East" (Ningrum, 2015). The sweet scent is contributed by the alkaloidic 2-acetyl-1-pyrroline. Among the earliest alkaloid variation was observed in the leaves of *P. amaryllifolius* that were collected from different sites such as Philippines, Thailand and Indonesia. Research by Nonato *et al*., (1993) showed three piperidine alkaloids which are pandamarilactones-1, -32 and -31. All of these piperidine alkaloids are derived biogenetically from 4-hydroxy-4-methylglutamic acid. From the literature, only one percent of the total *Pandanus* species were analysed in the studies related to their secondary metabolites (Mohsin, 2013). Other *Pandanus* chemical components include the aldehyde (Mai *et al*., 2015), carotenoids (Sarungallo *et al*., 2015), triterpenes (Inada *et al*., 2005) and phytosterols (Tan *et al*., 2008). Scientific publications offered neither a recent record of all *Pandanus* alkaloids, nor the suggestion of any classification of these biomolecules. Therefore, this paper is aimed to propose the unprecedented nomenclature of *Pandanus* alkaloids, following the inventory of their 26 natural alkaloids (Armayni, 2015).

Methodology

The references on *Pandanus*' phytochemicals, specifically their alkaloids, were reviewed. The electronic search was performed using collected English language articles until 2015. All chemical structures of the *Pandanus*' alkaloids were analysed. The basic alkaloidal moiety was then determined, in order to suggest the nomenclature of these alkaloids.

Results and Discussion

Table 1 displays all the isolated alkaloids from *Pandanus* species. It is observed that these specific compounds have a basic C_9-N-C_9 molecular framework (Figure 1) (Armayni, 2015; Mohsin, 2013).

Table 1: The alkaloids from *Pandanus* Species.

Pandanus	**Isolated alkaloids**	**References**
P. amaryllifolius (leaves)	Pandamarilactone-1 Pandamarilactone-31 Pandamarilactone-32	Nonato et al., (1993)
	Pandamarilactames-3x & -3y Pandamarilactonine-A & Pandamarilactonine-B	Sjaifullah et al., (1996) Takayama et al., (2000)
	Pandanamine	Takayama et al., (2001)
	Norpandamarilactonine-A & Norpandamarilactonine-B	Takayama et al., (2001)
	Pandamarilactonine-C & Pandamarilactonine-D	Takayama et al., (2002)
	6E-pandanamine & Two artifacts of pyrrolidine alkaloids	Salim et al., (2004)
P. amaryllifolius (roots)	Pandamarilactonine-E, Pandamarilactonine-F, Pandamarilactonine-F-*N*-Oxide, Pandamarilactonine-G & Pandamarilactonine-H	Tan et al., (2010b & 2010c)
P. dubius (leaves)	Dubiusamine-A & Dubiusamine-B	Tan et al., (2010a)
P. pygmaeus (leaves)	Pygmaeusamine-A & Pygmaeusamine-B	Mohsin (2013) Armayni (2015)
P. utilis (leaves)	Pandalisines A and B	Cheng et al., (2015)

For an example, in the arrangement of carbon atoms of Pandanamine (Takayama *et al*., 2001), the first carbon (C-1) is counted at the heteroatom of oxygen and the second carbon is attached with the ketone group. The C-1 to C-9 was assigned with one lactone skeleton. In the meantime, C-1' to C-9' or C-11 to C-19 showed the second lactone moiety.

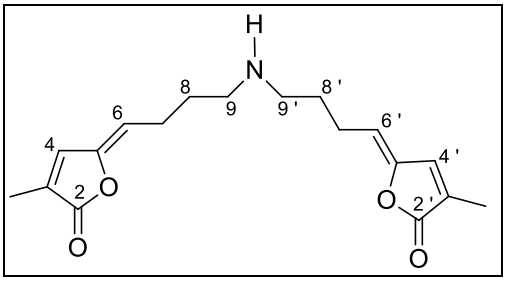

Figure 1: C_9-N-C_9 skeleton in pandanamine. It has two lactone rings and this might be observed in all alkaloids that were isolated from *Pandanus* species.

Furthermore, this nomenclature is determined based on its amine group. Pandanamine, being a symmetrical secondary amine, is hypothetically a biogenetic precursor of the *Pandanus* alkaloids. It has a straight chain of amino group that undergoes intramolecular cyclisation to form heterocyclic amines such as pyrrolidine (five-membered ring), piperidine (six-membered ring) and indolizidine (five- and six-membered rings). Thus, the compound that consists of piperidine alkaloid was named as pandamarilactone (Nonato *et al*. 1993) (Figure 2, 3).

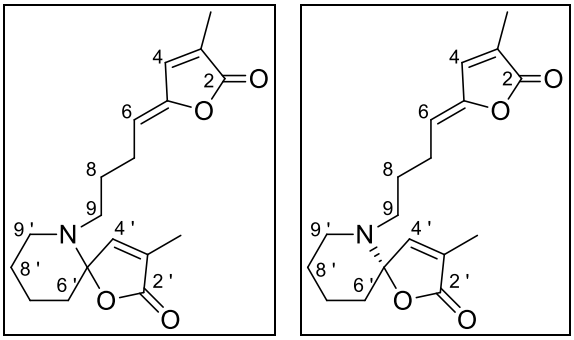

Figure 2: C_9-N-C_9 skeleton in pandamarilactone-1 (left) and Pandamarilactone-31 (right).

All of these piperidine alkaloids (Figure 2 and 3) are derived biogenetically from 4-hydroxy-4-methylglutamic acid. In addition, according to Peterson and Fowden (1972), leucin could possibly be the biogenetic origin of 4-methylglutamic acid, which was then converted to 4-hydroxy-4-methylglutamic acid. This compound is a suitable precursor for the five-membered ring structure that might cyclize to either lactone or lactam ring product.

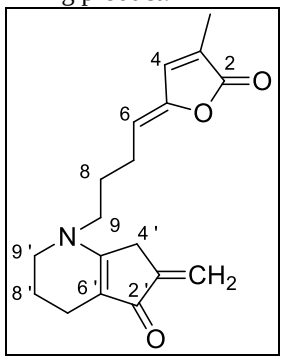

Figure 3: C_9-N-C_9 skeleton in pandamarilactone-32.

Meanwhile, the molecules having pyrrolidine alkaloid was referred as pandamarilactone. A study by Sjaifullah & Garson, (1996) indicated the presence of these pyrrolidinone-type molecules named pandamarilactam-3x and -3y (Figure 4), having the lactone moiety.

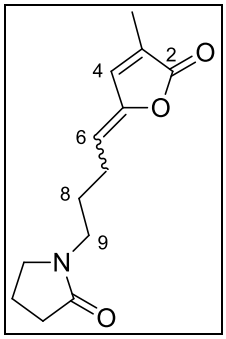

Figure 4: Pandamarilactam-3x and -3y.

From the same *Pandanus* species, Takayama *et al*., (2000) reported the isolation of two pyrrolidine alkaloids from the ethanol extract, which are pandamarilactonine-A and –B (Figure 5). The existence of pandanamine (Figure 1), a symmetrical secondary amine that was predictable as a common biogenetic precursor of pandamarilactone-1 (Figure 3) and pandamarilactonines-A, -B (Figure 5)**.**

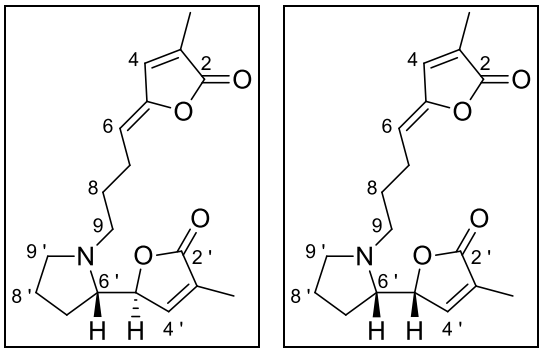

Figure 5: C_9-N-C_9 skeleton in pandamarilactonine-A & -B.

The nomenclature of this *Pandanus'* alkaloids were also applicable to two diastereomeric alkaloids which are norpandamarilactonines-A and –B (Figure 6). They are known as a norpandamarilactonines because they possess the substructure of pandamarilactonines-A and –B (Figure 5) and lack of a γ-alkylidene-α,β-unsaturated γ-lactone moiety.

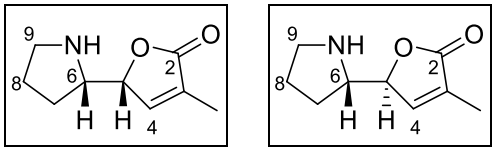

Figure 6: C_9-N-C_9 skeleton in norpandamarilactonines-A and –B.

Later, Takayama *et al*., (2002) also found two pyrrolidine alkaloids named pandamarilactonines-C and

–D (Figure 7) that indicated as the isomers of pandamarilactonines-A and –B (Figure 5). These four alkaloids are known as stereoisomers since they encompassed two skeletons which are γ-butylidene-α-methyl α,β-unsaturated γ-lactone and pyrrolidinyl-α,β-unsaturated γ-lactone skeletons.

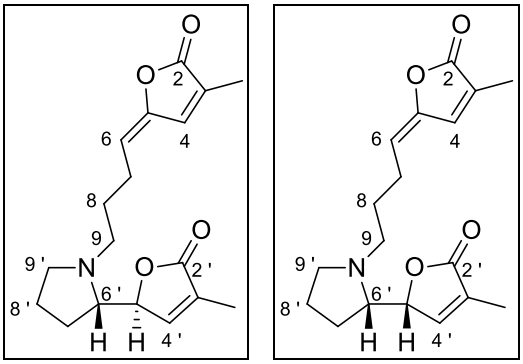

Figure 7: C_9-N-C_9 skeleton in pandamarilactonines-C and D.

According to Salim *et al*., (2004), *6E*-pandanamine (Figure 8) was isolated from ethanol leaves extract of *P. amaryllifolius*. This alkaloid is the *E* isomer for pandanamine (Figure 1) and differed only in the stereochemistry of C5-C6 and C5'-C6' double bonds.

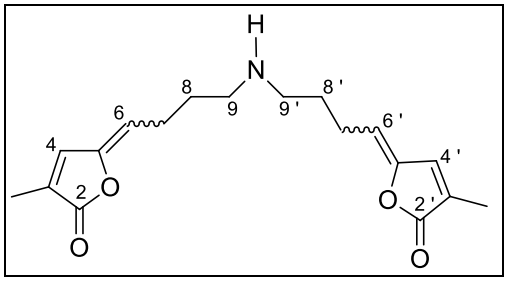

Figure 8: C_9-N-C_9 skeleton in *6E*-pandanamine.

The presence of alkaloids is not only detected in *P. amaryllifolius* leaves, but the constituent also can be found in the root part of *Pandanus* species. Research by Tan *et al*., (2010c) reported the existence of pyrrolidine-type alkaloids named pandamarilactonines-E, -F, -F-N-oxide, -G and also pandamarilactonine-H that were isolated from methanol extract (Figure 9, 10) (Tan *et al*., 2010b). These alkaloids comprised of a pyrrolidine moiety and two α-methyl-γ-lactone skeletons while pandamarilactonines-G (Figure 10) possesses a pyrrolidinone function. Pandamarilactonine-H was seen to possess a methyl-2-(pyrrolidin-2-yl) acetate function (Figure 10).

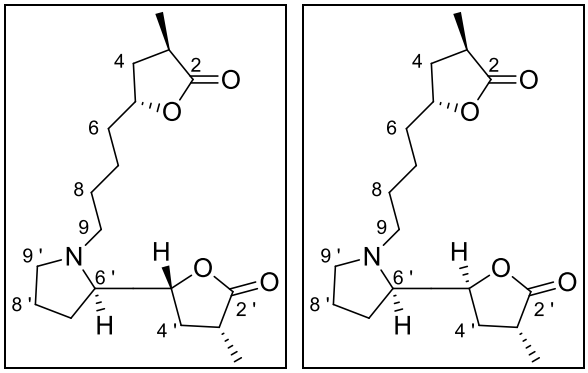

Figure 9: C_9-N-C_9 skeleton in pandamarilactonines-E and -F.

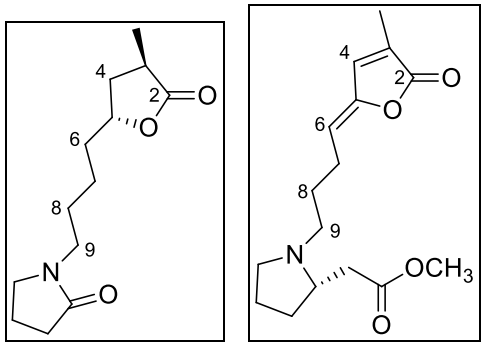

Figure 10: C_9-N-C_9 skeleton in pandamarilactonines-G and -H.

Another *Pandanus* species, which is *Pandanus dubius*, also contains alkaloids such as dubiusamines-A and –B (Figure 11), that were isolated from the methanol leaves extract. The method in carbon numbering was practised in both compounds as well. It was found that the nomenclature was in agreement with the formation of these two compounds, as could be seen originating from pandanamine (Figure 12).

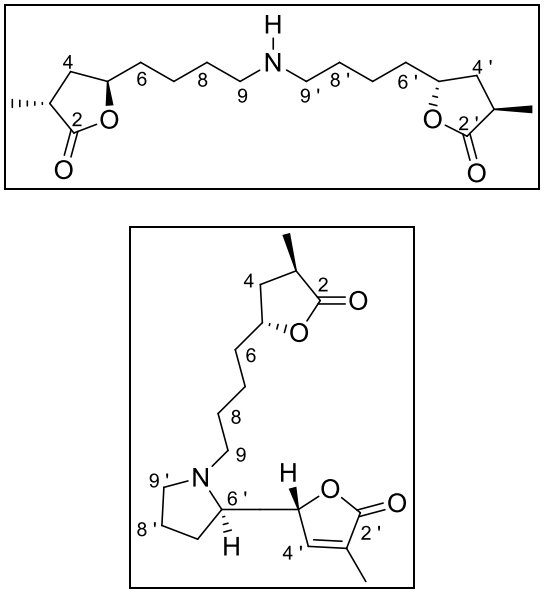

Figure 11: C_9-N-C_9 skeleton in dubiusamines-A (top) and –B (bottom).

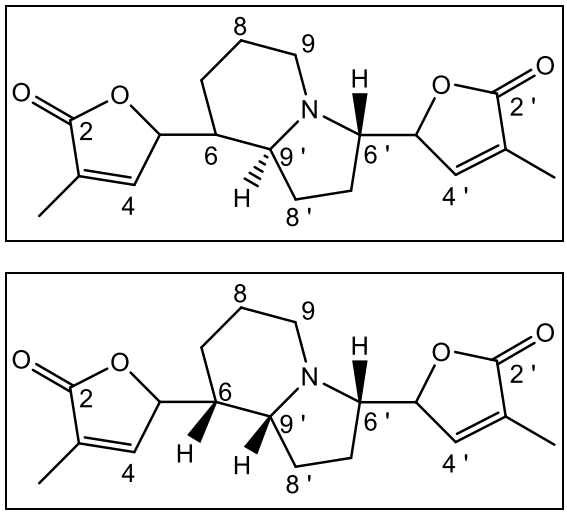

Figure 12: The indolizidine alkaloids, Pygmauesamine A (top) and its novel isomer, Pygmauesamine B (bottom) were isolated from *Pandanus pygmaeus* (Mohsin, 2013; Armayni, 2015).

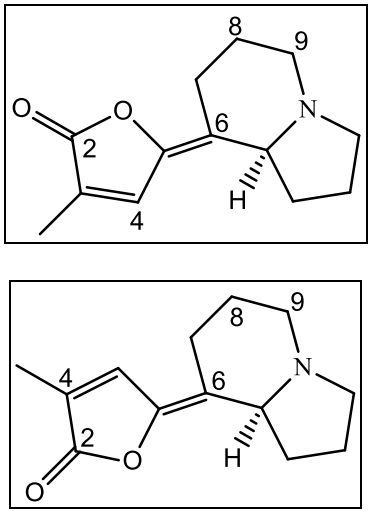

Figure 13: The second reported *Pandanus*' indolizidine alkaloids, Pandalisine A (top) and its isomer, Pandalisine B (bottom) from *Pandanus utilis* (Cheng et al., 2015). Note on the partial structural similarity with Pygmauesamine A and B (Figure 12).

Conclusions

From the literature review, the *Pandanus*' phytochemicals, especially their natural alkaloids, were examined, structurally. The search on the journals and scientific articles revealed the similarity of *Pandanus* species having nitrogenous compounds. All the chemical structures of these alkaloids were studied and re-drawn. The basic alkaloidal moiety was then determined, and the nomenclature of these alkaloids could be brought forward.

The proposed systematic classification of the above alkaloid was utilised as well, in order to characterise two novel alkaloids, Pygmauesamine A and B (Figure 12), which were purified from the dichloromethane extract of *Pandanus pygmaeus* (Mohsin, 2013; Armayni, 2015).

Such compounds owning the indolizidine ring might possess biological activities such as antibacterial, fungicidal and insecticidal properties. Nevertheless, the most recent result showed that Pandalisines A and B (Figure 13) are the first non-cytotoxic indolizidine alkaloids (Cheng *et al*., 2015). It is anticipated that the suggested nomenclature could be applied indefinitely, due to the relatively small number of *Pandanus'* alkaloidal structures.

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