

Medication development and chemical information

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ABSTRACT

Spermidine and spermine are unique polyamines found in living things. Putrescine and S-adenosylmethionine are created in the body through an enzyme-catalyzed process. Multiple amino groups are present in spermidine and spermine, which are also tightly linked to cell development, division, and survival. In plants, microorganisms, and marine species, spermidine and spermine alkaloids are extensively dispersed and can be categorized as macrocyclic and open chain compounds based on their skeletons.

The pharmacological effects of spermidine and spermine alkaloids included anti-inflammatory, antibacterial, anti-tumor, anti-Alzheimer's, and anti-viral properties. However, there haven't been many comprehensive reviews of spermidine and spermine alkaloids up to this point. We have outlined the distributions and pharmacological effects of spermidine and spermine alkaloids in this review based on the number of atoms in the ring.

INTRODUCTION

A type of substances known as polyamines contain two or more amino groups. Putrescine, spermidine, and spermine are the most prevalent polyamines with significant physiological roles. In all living things, spermidine (N-C3-N-C4-N) is present in large amounts and is produced by putrescine and S-adenosylmethionine. Spermine is a type of polyamine that has two primary and two secondary amines in its structure (N-C3-N-C4-N-C3-N). Putrescine and S-adenosylmethionine, which are catalyzed by a number of enzymes, produce it in living things. For cell viability, proliferation, function, and differentiation as well as biological activities like anti-aging and anti-cancer, spermidine and spermine are crucial. Plants, microbes, and marine life all contain spermidine and spermine alkaloids, which can be categorized as macrocyclic and open chain compounds based on their skeletons. The isomer of spermine that results from spermidine conversion is thermospermine. Alkaloids related to thermospermine are found in a variety of plants. Numerous pharmacological actions, including anti-inflammatory, antibacterial, anti-tumor, anti-Alzheimer's, and anti-virus, are displayed by the spermidine and spermine alkaloids. Even though spermidine and spermine alkaloids have been discovered in large quantities throughout the years, it is unclear what role they play in

chemophenetics. Since macrocyclic spermidine and spermine alkaloids are less well-reported than open chain spermidine and spermine alkaloids, it is important to learn about the distribution characteristics of these alkaloids. A class of amide alkaloids with a spermidine nucleus is known as dovyalycin-type alkaloids. This class of alkaloids has just recently been discovered in the genera *Dovyalis* (*D. abyssinica*, *D. macrocalyx*, *D. hebecarpa*, and *D. caffra*) and *Homalium* (*H. cochinchinensis*), of which nine members have been called dovyalycin A through I. The dovyalycins have three different types of skeletons. Dovyalycin A, B, C, E, G, H, and I all include spermidine as a component of a perhydro-1,5-diazocine moiety to create an 8-membered heterocyclic ring, while Dovyalycin D has spermidine as a component of a perhydro-1,4-diazepine moiety. Each of the dovyalycins (A, B, E, H, and I) has a C-4 phenyl. Dovyalycin A/N-5(-) methyl analogue of Dovyalycin E, Dovyalycin B C-4' methyl analogue of Dovyalycin A, and Dovyalycin H and Dovyalycin I C-4' trans and cis cinnamoyl analogues of Dovyalycin A, respectively, are different in N-5 and C-4' groups. Dovyalycin C is the dovyalycin A's 3-benzoyl counterpart; it lacks the C-4 substituted group. The 8-membered perhydro-1,5-diazocine ring of dovyalycin F, which possesses a lengthy side chain at the C-4' position, is unsubstituted. Dovyalycin D lacks optical rotation and is likely racemic since it has a perhydro-1,4-

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diazepine ring oxygenated at C-3 rather than the perhydro-1,5-diazocine ring. Dovayalicin F occurs as a combination of cis and trans conformers at room temperature. The groups *Celastraceae*, *Lamiaceae*, and *Fabaceae* have the majority of the 13-membered ring spermidine lactam alkaloids. Most of the 13-membered ring spermidine alkaloids differ in substituent groups of C-1 and C-8. At C-8, benzene and its derivatives are frequently substituted. The acyl side chain is the only distinction between celalocinnine, celacinnine, celafurine, and celabenzine. The existence of a 13-membered ring reflecting spermidine and cinnamoyl precursorial units at C-1 distinguishes celalocinnine and celacinnine from one another. The cinnamoyl double bond has a cis configuration for celalocinnine and a trans configuration for celacinnine, making them cis- and trans-isomers of one other. *Meehania fargesii* was used to isolate Meefarnine A and B, which had separate celalocinnine- and celacinnine-type skeletons. They are a pair of cis- and trans-isomers that are similar to celalocinnine and celacinnine. Pleurostylin is a structure in which spermidine is integrated into a 13-membered lactam ring, to which an extra cinnamoyl residue is fused to produce a 7-membered ring. It was isolated from the genus *Pleurostylia*. Two pleurostylin-type alkaloids, 7-hydroxypleurostyline and 7'-hydroxy-7',8'-dihydropleurostyline, as well as one celacinnine-type alkaloid, 7-hydroxycelacinnine, were isolated from *pleurostylia* opposite. These compounds show unique OH substitutions in the macrocycle or the 7-membered ring. A hydroxylated cinnamoyl residue is incorporated in the macrocyclic to

produce a 5-membered ring in the structure of caesalpinine A, the only known 13-membered spermidine alkaloid identified from the fabaceae family. Instead of a cinnamoyl group, celabenzine has a spermidine unit N1-linked to a benzoyl group. An N9-methylated celabenzine was discovered by Da Silva in *Gymnosporia arenicola* leaf. The three alkaloids cyclocelabenzine, isocyclocelabenzine, and hydroxyl-isocyclobenzine demonstrate how the benzoyl residue in the spermidine unit is connected to the celabenzine's 13-membered lactam ring. The first known spermidine alkaloid having a hydroxy function at the macrocycle is hydroxyisocyclocelabenzine. Only *Tripterygium wilfordii* contains a furan formate moiety, which is present in celafurine. Our team recently identified celecarfurine, a novel 13-membered spermidine macrocyclic alkaloid from the same plant. The macrocycle of celecarfurine has two amide carbonyls and is in the 2R-configuration. *Clerodendrum myricoides*, a member of the *Lamiaceae* family, and *Androea decaryi*, a member of the *Scrophulariaceae* family, both contain many spermidine alkaloids with no group connected to N-1. From *Clerodendrum myricoides*, myricoidine and dihydromyricoidine having an alkenyl bond to C-8 were identified. Dihydromyricoidine only has one carbon-carbon double bond, whereas myricoidine has two (both cis-configuration). From the leaves of *Androea decaryi*, two optical isomers (+)-decaryine A and (-)-decaryine B, as well as (-)-(2S)-2-phenyl-1,5,9-triazacyclotridecan-4-one, were isolated. A 13-membered lactam ring is fused to a 6-membered ring to form the structure that is represented by decaryine A/B. *Maytenus loeseneri* yielded loesenerine, N1-acetylated dihydromyricoidine, and two loesenerine-type spermidine alkaloids, 17,18-didehydroloesenerine and 16,17-didehydroloesenerin-18-ol.