I. Introduction

Ergot alkaloids are metabolites produced by a wide range of fungi, predominantly members of the grass-parasitizing family of the Clavicipitaceae. They are 3,4-substituted indol derivatives having a tetracyclic ergoline ring structure (Fig. 1). Based on their complexity, they can be divided into two families of compounds. In the \( \text{L-lysergic acid derivatives} \), a simple aminoalcohol or a short peptide chain is attached to the ergoline nucleus via an amide linkage or a carboxy group in the 8-position. In the simpler \( \text{clavine alkaloids} \), the carboxy group is replaced by a methyl or hydroxymethyl to which attachment of side groups such as in the amide-type alkaloids is not possible. Nearly always, the natural ergoline-derived alkaloids have a double bond in ring D of the tetracyclic ring system, either in \( \Delta 9,10 \) or \( \Delta 8,9 \), and the nitrogen in ring D is always methylated (Fig. 1).

The naturally occurring \( \text{L-lysergic acid amides} \), produced by the ergot fungus \( \text{Claviceps purpurea} \), have been used as medicinal agents for a long time. \( \text{L-lysergic acid} \) is a most potent pharmacophore when amidated at its carboxy group. Depending on the structure of the amide substituents, the carbon skeleton of the tetracyclic ring system can mimic the structures of dopamine/adrenaline or serotonine (Fig. 2). In each of its manifold natural and semisynthetic derivatives, the pharmacophore has a different affinity for its targets and may switch from agonist to antagonist behavior, depending on the receptor and its biochemical environment. Since the dopaminergic, adrenergic and serotoninergic receptor families themselves also have many members, each of which have different expression levels in the various tissues of the body, all these conditions explain the multitude of actions of this class of compounds, and leads to a broad specificity which can provoke undesired side effects.
Fig. 2. Structural analogy between the ergoline ring system and different neurotransmitters (dopamine, noradrenaline, serotonin). Peptide ergot alkaloids usually have high affinity to α-adrenergic receptors. Derivatives of d-lysergic acid amidated with small aminoalcohols show high affinity to serotonin receptors. Bromination of ergocryptine in the 2-position strongly increases the dopamine agonist activity.

Fig. 1. Structure of the ergoline ring system. The structures of some representative clavine alkaloids (top) and the general structure of d-lysergic acid amides (bottom) are given.