ESI-Mass spectrometric studies of the non-covalent complexes of hydrochlorides of arylpiperazine derivatives

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In recent years, electrospray ionization mass spectrometry (ESI-MS) has become an important tool in the field of biomedical research, providing valuable information on structurally specific biomolecular interactions. Since the ionization process, used in this method is very soft and leaves the ion mainly unfragmented, especially complexation involving non-covalent interactions of both large and small molecules can be studied.

The ESI-MS technique was applied in our laboratory to characterize the newly synthesized arylpiperazine ligands of serotonin 5-HT_{1A} receptors. Their general chemical structure consists of an alkyl chain (3–4 methylene units) attached to the N4 atom of the piperazine moiety, and a terminal amide or imide fragment. When those amines in the form of free bases were analyzed, their positive ESI-MS spectra contained only the respective pseudomolecular $[M+H]^+$ ion peak. In the case of their hydrochloride salts, however, also complex ions of more than doubled mass were often found. The same phenomenon was observed for the hydrochloride of buspirone – a well-known anxiolytic drug. It was found that these non-covalent complexes consisted of two protonated amines and one chlorine anion, and that the complexation process depended on structural features of the analyzed compounds (1).

In order to further explore “structure-complex formation relationships”, a set of arylpiperazine derivatives with a greater structural variability was investigated. Different (in size and nature) terminal fragments were used and studied in respect of the length (2–4 methylene units) of an alkyl linker. It was also found that the replacement of arylpiperazine moiety by an isosteric tetrahydroisoquinoline group did not influence complex ion formation.

(1) Kowalski P., Suder P., Kowalska T., Silberring J., Duszyńska B., Bojarski AJ. *Rapid Commun. Mass Spectrom.* **2003**; *17*, 2139–2146.