QUANTUM-MECHANICAL STUDIES ON THE EFFECT OF WATER ON THE CONFORMATION OF TWO BIOLOGICALLY IMPORTANT ZWITTERIONIC SYSTEMS: POLAR HEAD OF PHOSPHOLIPIDS AND GABA

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1. Introduction

In the preceding symposium of this series [1] we have presented results of quantum-mechanical computations on the effect of water on the conformational properties of a large number of pharmacological compounds of the arylethylamine type: (histamine, indolealkylamines, phenethylamines etc.) in their cationic form considered generally as the most significant one from the biological point of view. In the present communication we extend our investigation to two biologically important *zwitterionic* systems: the polar head of the phospholipids and the important central nervous system transmitter GABA (γ-aminobutyric acid).

In these studies the computations for the isolated molecules are carried out by the PCILO (Perturbative Configuration Interaction using Localized Orbitals) method [2, 3] and by the SCF *ab initio* procedure using the program Gaussian 70 [4] with an STO 3G basis set [5]. The influence of water on the conformation of the zwitterion is studied by the 'microscopic supermolecular' approach, which consists of fixing water molecules at the most favorable hydration sites and calculating the conformational map of the new 'supermolecule'. The most favorable hydration sites are determined by *ab initio* studies on model compounds, following the procedure indicated in References 6–10 and recently reviewed in [11]. The conformational map of the new supermolecule, representing the hydrated species, is computed by the PCILO method alone, as the hydrated compound is too large for computations *ab initio*. As discussed in papers [6–11] it is not expected that the entire solution behaviour of molecules will be explained by the reduced treatment considered here. It is, however, assumed that this approach may yield a reasonable indication of the direction and magnitude of changes in conformational preferences of the isolated molecule as it enters aqueous solution and that from that point of view the inclusion of the essential water molecules of the first hydration shell should be particularly significant, especially in cases in which these molecules are very strongly bound to polar groups of the substrate. This expectation was fully satisfied by the comparison of theory with experiments in the groups of compounds studied so far [1]. It is therefore expected that the procedure should give significant results in the case of the presently considered zwitterionic systems also.