Mass spectrometric investigation of diazepam derivative drugs using electronionzation[ei]and chemical ionization[ci]technicques

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A mass spectrometer of the type QMS (SSQ710) is used to record electron ionization and chemical ionization mass spectra for diazepam and three of its derivatives namely, tetrazepam, bromazepam and clonazepam.In EI mass spectra of the four compounds, the molecular ions have two peaks at m/z [M]+• and [M+2]+• due to the natural ratio of the isotopes (37Cl/35Cl = 1:3) for diazepam, tetrazepam and clonazepam and (81Br/79Br = 1:1) for bromazepam.The relative intensities at different electron energies (15, 20,30,40,50 and70 eV) for the prominent ions in the EI mass spectra of the studied compounds are reported and discussed. Also, fragmentation patterns for the four compounds have been suggested and discussed and the most important primary fragmentation processes such as [M-H]+, [M-X]+ (X= Cl or Br) and [M-CO]+• are investigated.On the other hand, chemical ionization (CI) mass spectra of the compounds have been recorded using methane as the reagent gas. These spectra are discussed in terms of the structure of the compounds, with particular reference to their conventional electron ionization mass spectra. The protonated molecule [M+H]+ is stable and more relatively abundant in the chemical ionization (CI) mode than the molecular ion[M]+• in electron ionization -mode. Both spectra show structural data information.Using the MNDO semi empirical method for computation together with experimental results gives valuable information about heats of formation and ionization energies of the molecules. The effect of substituent on the geometry of the neutral and ionized molecules are reflected in the values of the ionization energy and heats of formation of neutral and ionized molecules. The calculated values of ionization energies for diazepam, tetrazepam, bromazepam and clonazepam are 8.35, 8.39,8.22 and 9.12 eV ,respectively. The ionization may be due to the removal of one of the lone pair electrons of nitrogen (N1 or N4) or oxygen (O19) atoms in the seven member ring of the benzodiazepine. These values of ionization energies are not published yet. Also, the calculated heats of formation of neutral and ionized molecules are discussed and were found to depend on the difference in the substituents of the different molecules.Furthermore, molecular orbital calculations (MNDO) is also used to probe the protonation of these compounds. Proton affinities (PA’s) of the compounds at nitrogen (N1 / N4) atom and at oxygen(O19) atom are calculated and the results show some interesting features for the protonation sites. Protonation at nitrogen —N4 and oxygen —O19 sites are slightly more favored than that at nitrogen —N1

for the compounds under investigation and the PA’s at both —N4 and —O19 have similar values. Also, the calculated heats of protonation for the four compounds at N4 and O19 are lower than that at N1. This indicates that the protonated ions at sites N4 and O19 are to be more stable than at site N1 for all the compounds studied. i.e. the results indicate that protonation occurs on N4 and O19 .All the calculated values of the heats of formation of neutral [M], ionized [M]+• and protonated molecule [M+H]+ and PA’s values are reported for the first time.