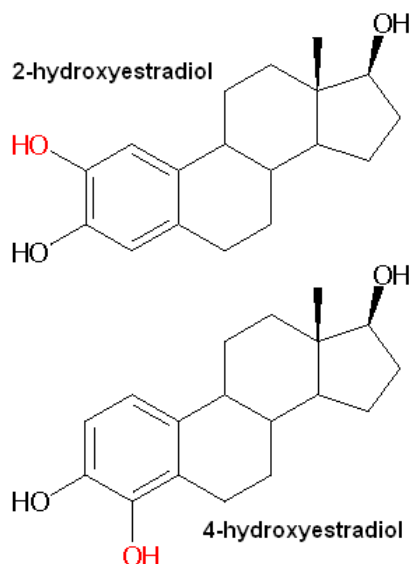


Improved Mass Spectrometry for Analyzing Catechol Estrogen Varieties



DESCRIPTION

Electrospray Mass Spectrometry (ES-MS) is a valuable tool in examining complex molecules and mixtures, particularly when coupled with liquid chromatography to improve separation of different molecules. ES converts large molecules into ions, then MS separates the ionized fragments based on their mass-to-charge ratio; the resulting spectrum provides a signature that can be used to identify known compounds or help characterize new ones. Peptide sequencing has long been enabled by MS, however the method remains limited by an inability to capture all information about post-translational modification of proteins, for example the addition of carbohydrates to glycoproteins. The ionization of such proteins results in spectra where subtle differences in structure, such as isomers of the same molecular formula, are undetectable.

City of Hope has developed a novel technology for detecting these subtle, but notable differences in post-translational protein structure. The method uses ferrocene boronic acid to modify compounds in the sample mixture; these ferrocenyl boronate labeled derivatives have an increased ability to ionize and they ionize into unique, recognizable fragment distributions for each of the different isomers in the sample. This has a valuable application in understanding cancer progression. The development of malignant breast cancer and prostate cancer has been associated with increased levels of “bad” estrogen (4-hydroxyestradiol) while “good” estrogen (2-hydroxyestradiol) appears to have anti-cancer protective effects. Using conventional ES-MS, these two forms of estrogen are indistinguishable from one another. This technology creates a method for identifying both forms and evaluating the relative ratio of these isomers in patient samples, thus providing a diagnostic tool to improve our understanding of the relationship between these two molecules and disease states.

KEY ASPECTS

- Ferrocenyl boronate treatment of catechol estrogens generates differences in the electrospray-mass spectroscopy fragmentation spectra for different isomers
- Provides a means of measuring the relative ratio of “good” estrogen (2-hydroxyestradiol) to “bad” estrogen (4- in the context of malignant cancer pathogenesis)

INTELLECTUAL PROPERTY

Title	US Patent Number	Issued
Ferrocenyl Boronate Derivatization of Chemical Compounds Undergoing Mass Spectrometry Analysis	6,734,024	5/11/2004

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