comply with its rules.

11:55 Oral

Ligand-directed receptor trafficking

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Receptors are areas of certain proteins and glycoproteins which are conveying different stimuli upon activating by specific ligands. Activating of a receptor enables a signal transduction pathway usually by activating specific proteins. Receptors which bind G proteins upon activation are called G protein-coupled receptors (GCPRs). According to the traditional two-state model of receptor theory, GPCRs were considered as operating in equilibrium between two functional conformations, an active and inactive state. It also was thought that GPCRs were to activate only G proteins to induce response. More recent data show that numerous other signalling proteins, such as β-arrestins and phosphorylating enzymes, may interact with GPCRs and activate different intracellular signalling pathways. This also may involve pathways that are independent of G proteins. Various ligands that affect GPCR in a different way and activate specific signalling pathways have been discovered that gave rise to a concept called (among others) ligand-directed receptor trafficking. A ligand might act as an agonist for one signalling pathway while behaving as an antagonist, partial agonist, or have no effect for another signalling pathway. Side effects can arise not only because of the drug binding to different receptors but also by activating different signalling pathways of the same receptor. Challenge for new drug development may therefore not only be to discover compounds with high receptor specificity, but also compounds that can distinguish between the signalling pathways of a particular receptor.

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12:15 Oral

Shimadzu solutions for the pharmaceutical science; A. High speed drug screening and quantification. B. Evaluation of pills by compression and splitting tests

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A. In the different phases of drug development, metabolites need to be screened on a regular basis. In the early stage where the number of samples screened is still relatively low, the focus is mainly on sensitivity. However, it shifts in general to higher throughput with the demand for moderate sensitivity at a later stage. In order to be able to fulfill this demand, the analytical solution needs to be reliable on the HPLC as well on the MS whereas a one hand supplier solution has a number of advantages. Fast separation, resulting in narrow peak width, requires the acquisition of enough data points over a peak to be able to generate accurate information for quantification as well as generating product ion scans for further confirmation. In addition to the required fast scan speed the polarity switching is an important feature as well to shorten run time without sacrificing the level of information generated. The demand of low dwell and pause time may be important if a large number of MRM transitions (Multiple Reaction Monitoring) are relevant to screen. In this context, a low cross talk between the different MRMs is important to avoid contamination between the different identification steps as well as an error in the quantification.

26 pharmaceutical compounds were analyzed using Shimadzu's Synchronized Survey Scan (SSS). In this mode full scan measurement is rapidly followed by automated product ion scanning. High-speed polarity switching (15 msec.) and rapid scan rates (15,000 u/sec.) allow multiple collision energies to be employed for unknowns even with narrow peak widths. This enables molecular weight confirmation from the Q3 scan data and also generates structural fragmentation information from the same peak. A total of 26 pharmaceutical compounds were evaluated. All compounds were detected in either positive mode, negative mode or both, demonstrating the LCMS-8030's effectiveness for drug discovery and synthesis confirmation.

B. Many tablets have groove in the center, allowing them to break accurately in half. The tests performed on the universal testing machine – Shimadzu's EZ-TestX with the appropriate 3-point bending jig, made possible to obtain the force parameters connected with breaking the tablet. Test force measurement and visual inspection of the specimen after the breakage have crucial meaning in optimization of groove depth. Another important use of the EZ-TestX machine is the test performed by pushing the tablet out of PTP package using spherical test jigs. Maximum test force needed to push the tablet out is important parameter for quality control and product development.

12:35 Oral

Glucuronidation of antitumor agents - detoxification, mechanism of drug resistance or the prodrug design? Studies on acridine antitumor agents in the light of clinical therapeutics

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Glucuronidation, representative of II phase of metabolism, is a crucial pathway of metabolism and excretion of endogenous compounds and xenobiotics. UDP-glucuronyltransferases (UGT; EC 2.4.1.17) catalyse transformation of bilirubine, steroids and thyroid hormones, bile acids as well as exogenous compounds, including drugs, carcinogens, environmental pollutants and nutrient components. Deactivation of xenobiotics and the following excretion of hydrophilic conjugates should be a main task of glucuronidation.