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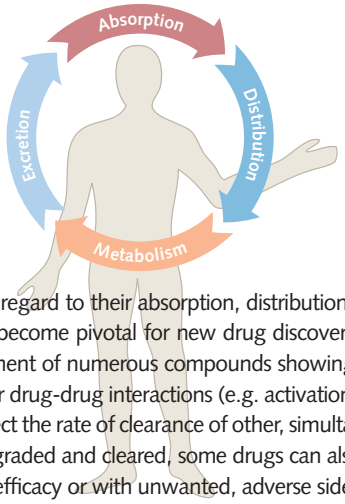

Drug Discovery & Development
Assays for Drug Testing

All newly developed drugs coming onto the market have been tested with regard to their absorption, distribution, metabolism and excretion/clearance (ADME testing). Thus, early evaluation of pharmacokinetics has become pivotal for new drug discovery and lead optimization and considerable effort is expended in new drug research to avoid the development of numerous compounds showing promising pharmacological activity but will eventually fail for reasons related to bioavailability, toxicity, or drug-drug interactions (e.g. activation/inhibition of CYP proteins). In addition to affecting its own metabolism and clearance rate, drugs can affect the rate of clearance of other, simultaneously administered drugs, causing severe or even fatal drug-drug interactions (DDI). Besides being degraded and cleared, some drugs can also be activated - primarily by liver CYP450 enzymes - to form potent metabolites either with the desired efficacy or with unwanted, adverse side effects.

Liver Metabolism/Clearance Assays

The liver is the main site of metabolism clearance and most drugs are cleared by CYP proteins which are responsible for Phase I biotransformation reactions, in which lipophilic drugs and other xenobiotic compounds are transformed to more hydrophilic products to facilitate excretion from the body. Drugs can decrease but also increase the activity of one or more CYP enzymes, which alters the rate at which the drug is degraded and cleared from the body. That can render the drug ineffective or may not prevent the drug from accumulating to toxic levels. The most common mechanism underlying drug-drug interactions is the inhibition of cytochrome P450 activities. Thus, new drug candidates have to be tested against cytochrome P450 enzymes in several ways. Among the different CYP proteins, CYP1, CYP2, CYP3 and CYP4 are the most important in terms of drug biotranformations, especially CYP3A4, which is the most prevalent CYP in the body and metabolises several drugs.

Our **Cytochrome P450 (CYP) Activity Assay Kits** enable rapid measurement of native or recombinant CYP activity in biological samples such as *liver microsomes*. The assays utilize a non-fluorescent CYP substrate that is converted into a highly fluorescent metabolite detected in the visible range, ensuring a high signal-to-background ratio with little interference by autofluorescence.

Our **Cytochrome P450 Reductase (CPR) Activity Assay Kit** accurately and sensitively measures CPR activity by coupling oxidation of NADPH by CPR with reduction of a nearly colorless probe into a brightly colored product, with the rate of color generation being directly proportional to the CPR activity.

PromoKine's **Cytochrome P450 (CYP) Screening Kits** enable rapid screening of drugs and other new chemical entities (NCEs) for compound-CYP interaction in a reliable, high-throughput assay. The kits provide a yeast microsomal preparation of human CYP and cytochrome P450 reductase (CPR) enzymes and the assays utilize a non-fluorescent CYP substrate that is converted into a highly fluorescent metabolite, ensuring a high signal-to-background ratio with little interference by autofluorescence.

Uridine diphospho-glucuronosyltransferases (UGTs) are responsible for the vast majority of Phase II biotransformation (conjugation) reactions, in which a hydrophilic moiety is attached to small molecule drugs and other xenobiotics to facilitate their rapid excretion from the body.
PromoKine's **UGT Activity Assay / Ligand Screening Kit** enables rapid measurement of native or recombinant UGT activity in biological samples such as *liver microsomes* and can also be used to assess the effect of drugs and other novel compounds on UGT activity.

Microsomes are spherical vesicle-like structures formed from membrane fragments following homogenization and fractionation of eukaryotic cells. Microsomal preparations are an affordable and convenient *in vitro* system for assessing Phase I biotransformation reactions, as they contain all of the xenobiotic-metabolizing CYP isozymes and the membrane-bound flavoenzymes required for function of the multicomponent P450 enzyme system. Thus, microsomes isolated from liver tissue are used extensively in pharmaceutical research and environmental science to study the metabolism of drugs, organic pollutants and other xenobiotic compounds by the cytochrome P450 (CYP) enzyme superfamily.
PromoKine's **Microsome Isolation Kit** enables preparation of active microsomes in about one hour, without the need for ultracentrifugation or sucrose gradient fractionation. The kit contains sufficient reagents for simple and convenient procedures, yielding microsomes from roughly 25 grams of tissue or cultured cells.

Drug/Metabolite Transporter Assays

P-glycoprotein (P-gp, Multidrug Resistance Protein 1, MDR1) is an ABC transporter capable of transporting a vast array of neutral and anionic lipophilic molecules. It strongly affects the oral absorption, tissue distribution and excretion of many drugs, and prevents certain lipophilic drugs from penetrating the blood brain barrier. Overexpression of P-gp confers tumor cells with resistance to chemically and pharmacologically distinct chemotherapeutic drugs and and tumor-targeted delivery of P-gp inhibitors might be a strategy for overcoming chemotherapy resistance.

PromoKine's **MDR1/P-gp Ligand Screening Kit** is designed for rapidly screening test compounds for modulation of efflux transporter activity in MDR1-expressing cells. This highly sensitive, fluorometric assay has a simple no-wash protocol and is high-throughput adaptable.

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Renal Clearance Assays

There are three main sites where drug clearance occurs (kidney, liver and lung) and the kidney is the most important site where products are excreted. Consequently, for many drugs the clearance is simply considered as the renal excretion ability, i.e. the rate at which substances (e.g. drug metabolites) are cleared from the blood by the kidney. Clearance is a measure of kidney function describing the flow rate of filtered fluid through the kidney. Unless excretion is complete, accumulation of foreign substances can adversely affect normal metabolism and health.

Creatinine, a breakdown product of creatine phosphate, is produced and excreted at a constant rate. Blood creatinine is commonly used to determine the glomerular filtration rate (GFR), and creatinine clearance is a common means of standardizing excretion of other compounds. Based on creatinine clearance results, dosage of drugs excreted primarily via urine can be adjusted.
Inulin and Cystatin C clearance are alternative methods to determine the filtering capacity of the glomeruli.

The PromoKine **Creatinine Assay Kit** provides an accurate, convenient colorimetric and fluorometric method to measure creatine concentration in biological fluids such as serum, urine or CSF. Unlike the picric acid assay, this kit is suitable for serum/plasma creatinine determinations, as well as for urine and other biological samples.

The **Cystatin C ELISA Kit** is quantifying serum cystatin C that is considered as an alternative marker for renal clearance.

Our **Albumin-to-Creatinine Ratio (ACR) Assay Kit** provides a simple, sensitive, and high-throughput adaptable assay that detects albumin, creatinine, and the albumin-to-creatinine ratio, showing a wide detection range.

PromoKine's **Inulin Assay Kit** allows determination of inulin in biological fluids such as serum. The kit utilizes an enzymatic mechanism generating a fluorescence signal which is proportional to the amount of inulin present in the sample, allowing to quantify levels of inulin down to 10 ng.

Catalog Number	Product Name	Size
Liver Metabolism/Clearance Assays		
PK-CA577-K700	Cytochrome P450 Reductase (CPR) Activity Assay Kit	100 assays
PK-CA577-K701	Cytochrome P450 3A4 (CYP3A4) Activity Assay Kit	200 assays
PK-CA577-K702	Cytochrome P450 3A4 (CYP3A4) Inhibitor Screening Kit	200 assays
PK-CA577-K703	Cytochrome P450 2D6 (CYP2D6) Activity Assay Kit	200 assays
PK-CA577-K704	Cytochrome P450 2D6 (CYP2D6) Inhibitor Screening Kit	200 assays
PK-CA577-K848	Cytochrome P450 2C19 (CYP2C19) Activity Assay Kit	100 assays
PK-CA577-K849	Cytochrome P450 2C19 (CYP2C19) Inhibitor Screening Kit	100 assays
PK-CA577-K893	Cytochrome P450 1A2 (CYP1A2) Activity Assay Kit	100 assays
PK-CA577-K894	Cytochrome P450 1A2 (CYP1A2) Inhibitor Screening Kit	100 assays
PK-CA577-K895	Cytochrome P450 2C9 (CYP2C9) Activity Assay Kit	100 assays
PK-CA577-K896	Cytochrome P450 2C9 (CYP2C9) Inhibitor Screening Kit	100 assays
PK-CA577-K983	Aromatase (CYP19A) Activity Assay Kit	100 assays
PK-CA577-K984	Aromatase (CYP19A) Inhibitor Screening Kit	100 assays
PK-CA577-K249	Microsome Isolation Kit	50 assays
PK-CA577-K692	UGT Activity Assay / Ligand Screening Kit	100 assays
Renal Clearance Assays		
PK-CA577-K625	Creatinine Assay Kit	100 assays
PK-CA577-K551	Albumin-to-Creatinine Ratio (ACR) Assay Kit	100 assays
PK-CA577-K737	Inulin Assay Kit	100 assays
PK-EL-69050	Human Cystatin C ELISA	96 tests
Drug/Metabolite Transporter Assays		
PK-CA577-K507	MDR1/P-gp Ligand Screening Kit	100 assays

More cell metabolism assays as well as kits for drug screening/testing and for determining cell viability/proliferation, (drug) cytotoxicity/toxicology and necrosis/apoptosis can be found on our website **www.promokine.info**.

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