Application Guide

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Sartorius Cubis® Premium Balances:
Laboratory weighing applications in the fields of Biopharma, Pharma, Biomedical Sciences and Chemical engineering.

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Abstract

Laboratory analytical balances are crucial instruments used in various interdisciplinary fields of academic research. Remarkable developments achieved in recent years concerning both the technology and electronics of the weighing systems made research workflows easier and more efficient. Sartorius Cubis® line is the performance benchmark in its field. It offers attractive built-in- (e.g. calibration or leveling) and customizable software solutions (e.g. apps), modularity, web services and various connectivity options at the highest levels of accuracy and precision. In this guide you will find an overview of various weighing applications from the fields of biopharma, pharma, experimental medicine and chemical engineering published in peer reviewed academic journals.

Introduction

Biopharma, Pharma and Biomedical sciences
Biomedical and pharmacological sciences are a heterogeneous and highly dynamic fields spanning the entire spectrum of drug discovery and development. Using genetics, cellular – and molecular biology, immunology, neuroscience etc. the aim is to understand the cellular, molecular and physiological mechanisms underpinning the human health and disease states. Accurate and precise weighing is required in many important and decisive applications at various stages of the overall process. These applications are highly diverse and cover a wide range, including sample weighing, analytical standard preparations, nanoparticle weighing, loss of mass measurements, mass uniformity evaluations etc.

When we consider analytical standard preparations, working below the microgram (µg) range requires an extremely sensitive weighing instrument. For example in the case of the oral and intravenous drug administration routes, the exact parameters (e.g. plasma concentration after intravenous administration, ADME) of drug behavior cannot be properly evaluated real time. This hinders the prediction of drug behavior parameters, and the guidance of real time clinical dosing. Thus, reliable calibration and analytical validation techniques are necessary, like the recently developed highly innovative zebrafish study[23] showcases, where the whole-body uptake of pharmaceuticals was examined. Likewise, in the case of humans, novel calibration techniques for qualification of anesthetic drugs in breath[24] were validated. For this, the calibration standards and the pharmaceuticals have to be gravimetrically determined at the level of 0.1 µg readability (ultra-micro balance).

High sensitivity ultra-micro balances are also used for sample weighing for matrix sublimation, which is an essential prerequisite in SIMS, MALDI imaging experiments[4, 13, 27]. This is important when studying for example label-free biomolecules with high spatial and mass resolution[11], or in liquid chromatography-tandem mass spectrometry (LC-MS) for standard solution preparations[18].

Another high-end application is the gravimetric determination of purified nanoparticles which are used to encapsulate chemotherapeutic drugs for better therapeutic efficacy and lower toxicological effects[2].

As microbial resistance to antibiotics became a global problem, there is an urgency to develop new antimicrobial agents. Echinoderms have proven to be a great source of novel antimicrobial agents, delivering promising candidates for new antibiotic drug developments. As part of this process, coelomic fluid is obtained from the animals (in this case from Echinoderms in order to analyze the antimicrobial properties of coelomocytes), where a Cubis MSA model is used for the weight determination[9] of the coelomic fluid.

Further examples for diverse applications of Sartorius Cubis® laboratory balances in the field of biopharma, pharma and biomedical sciences you can find in Table 1.

Table 1: Sartorius Cubis® laboratory balances: Applications in Biopharma, Pharma and Biomedical Sciences

Field	Topic	Details	Type of Sartorius Cubis® Balance	Application	Reference
Biopharma | Nanomedicine	chemotherapy (cancer treatment)	Investigation of in vitro release profiles of b-cyclodextrin -nanoparticles as carrier for the chemotherapeutic drug idarubicin	Cubis®-Precision Balance	Dried weight determination of nanoparticles	1
Pharma | Biopharma	chemotherapy (cancer treatment)	Validation of a new chromatographic separation method to quantify paclitaxel (the most effective antitumor agent) in oil based nanomedicine drug delivery system	Cubis®-MSA-224S-000-DU-Analytical Balance	Preparation of analytical standards	2
Pharma | Drug Development	Natural source of novel antimicrobial agents	Isolation and characterization of antimicrobial peptides from Echinus esculentus	Cubis®-MSA Balance	Sample weighing of coelomocytes	9
Pharma | Quantitative Bioanalysis	Novel device for dried blood microsampling	Volumetric absorbtive microsampler (VAMS) for dried blood sampling was designed and tested	Cubis®-Micro Balance	Cross-company and – laboratory gravimetric experiment to determine the blood absorbed by the VAMS	10
Biopharma | Imaging	Imaging of labelfree biomolecules in single cells and subcellular organelles	C60-SIMS | MALDI offers imaging of intact biomolecules with high spatial- and mass resolution	Cubis®-Ultra-Micro Balance	Weighing of samples on silicon tiles in matrix sublimation	11

Field	Topic	Details	Type of Sartorius Cubis® Balance	Application	Reference
Medicine | Orthopaedy	A hip joint simulator study on standard vs cross-linked polyethylene	Comparison of gravimetric and micro-CT wear loss measurements (volume, distribution and deformation) of different polyethylene´s acetabular cups used in hip arthroplasty	Cubis®-MSE-225S-000-DU-Semi-Micro Balance	Determination of the wear mass loss of the acetabular cups	17
Medicine | Nephrology	Urinary lipids, as novel diagnostic markers in renal diseases	Clarification of the relevance of urinary cholesteryl ester in renal disease using liquid LC-MS	Cubis®-Ultra-Micro Balance	Dry weight determination and standard solution preparation of cholesteryl ester	18
Medicine | Pediatrics	Neonatal blood culture: volume optimalization	To reduce the sample volume of blood in sick neonates is important to avoid anemia. In this study it was proved that allocating 1 mL of blood into one aerobic and one anaerobic bottle imporved the yield of the culture.	Cubis®-Precision Balance	Blood culture bottle weighing	19
Medicine | Pediatrics	Improvement of sleep disturbances in autistic children	Dose-effect relationship of melatonin on sleep-patterns of autistic children	Cubis®-Balance	Mass uniformity evaluation of melatonin hard capsules	20
Medicine | Nephrology	Validity examination of physical activity questionnaries to estimate total energy expenditure in subjects with chronic kidney disease (CKD)	To estimate total energy expenditure in patients with CKD, Recent Physical Activity Questionnaire (RPAQ) method was validated against double-labelled water.	Cubis®-Analytical Balance	Sample measurement	21
Medicine | Pediatrics	Satiety regulation in children with loss of control (LOC) eating- and attention-deficit | hyperactivity disorder (ADHD) disorder	Examination of hunger and satiety regulation in children with LOC and ADHD disorder.	Cubis®-MSU-5201S-000-Precision Balance	Weighing of the nutrients placed on an universal eating monitor	22
Pharma	In vivo high-throughput screening to study the whole-body uptake of pharmaceuticals	Zebrafish, as a new in vivo model for Absorption, Distribution, Metabolism, and Excretion (ADME) studies.	Cubis®-Ultra-Micro Balance	Sample preparation of pharmaceuticals	23
Medicine | Anaesthesiology	Validation of different calibration techniques to improve the titration of anesthetic drugs	Liquid- and gaseous calibration techniques were validated for propofol quantification in breath in order to real time guide the clinical dosing of anesthetic drugs.	Cubis®-Analytical Balance	Determination of the exact mass of injected propofol	24
Medicine | Opthalmology	Investigation of the origin of the subretinal optic pit fluid	Subretinal optic pit fluid and cerebrospinal fluid) are not identical based on the results using bTP as a biomarker	Cubis®-Micro-Balance	Measurement of the volume of SRF and CSF samples	14
Medicine | Nutrition Research	Effect of portion size on meal eating parameters (e.g. bite size)	Bite size, eating rate, deceleration rate and meal duration were monitored with the Sussex Ingestion Pattern Monitor (SIMP) to investigate the effect of portion size in these eating parameters	Cubis®-Balance	Concealed scale integrated into SIPM and connected to a PC to measure meal eating patterns	16
Medicine | Endovascular Therapy	Development of a new catheter prototype for laser thrombolysis	Safety, efficiency and accuracy evaluation of a new catheter prototype combined with laser ablation and OCT imaging for the treatment of thrombolisis	Cubis®-Precision Balance	Following the thrombus size analysis experiments all thrombi were weighed.	15

Chemical engineering

Chemical engineering is a discipline influencing numerous industries (biotechnology, pharmaceuticals or environmental engineering). Taking interdisciplinarity to the next level, it combines life -, and physical sciences with applied mathematics and economics to transform and | or produce chemicals, materials, living cells, energy etc. into novel forms with altered functionality, and innovative products[12]. Among the broad range of applications[33] (solution preparation- and water content determination in Karl-Fischer Titration, binary mixture preparation and concentration determination, density determination, solubility- and swelling ratio measurements etc.) used for these technological processes, an accurate and precise mass determination is critical for successful experimentation.

For example, the presence of contaminants like pharmaceuticals in the environment is prompting the search for new methods in wastewater treatment in order to concentrate and remove them from soils, sediments, and effluents[28,29]. To achieve this, novel biocompatible aqueous biphasic systems have been designed for extracting non-steroidal and anti-inflammatory drugs from aqueous streams[5,6]. These systems are trending, because of their content of a myriad of anions and cations (acting as salting out agents), which opens up countless possibilities. During characterization of the aqueous biphasic systems, the solubility data needs to be obtained. This is done by mixing known amounts of the surfactant and ionic liquid in a dry chamber, covering the entire mass fraction range, where the precise determination of the concentration of these points requires semi-micro balances with a readability of 10 mg.

Another challenge in this field is the isolation of biotechnology-derived products from the medium. The interest in biomass-derived chemical products is permanently growing. Several studies considered integrating an in-situ liquid-liquid extraction step into the total production processes, in order to separate the desired product form the reaction medium[31]. However, electrolytes are known to have a strong influence on the mutual solubility of water and organic solvents as well as on partitioning of a product between water and the organic solvent. Thus, the systematic study of the salt effects on liquid-liquid equilibria (LLE) of involved liquid mixtures is a prerequisite for the design of extraction separation processes[32]. All the components used for the determination of the LLE data requires precise gravimetric determination. Further, the water content has to be determined as well, classically by Karl-Fischer titration, where an analytical balance is directly connected to the titrator[3,25].

An important aspect of environmental science and at the same time a challenge in the field of chemical engineering is to stabilize and prolong the lifetime of cassava based films (CBF), via increasing their resistance to chemical reactions. CBF have a great potential in the replacement of non-biodegradable plastics, because they can be broken down by natural processes, leaving no byproducts as waste, and are economically feasible. Film solubility- and swelling ratio measurements, as well as absorption testing of CBF requires gravimetrical tests as well[8].

For a more detailed overview of publications using Sartorius Cubis® laboratory balances in the fields of chemical engineering please refer to Table 2.

Table 2: Sartorius Cubis® laboratory balances: Applications in Chemical Engineering

Field	Topic	Details	Type of Sartorius Cubis® Balance	Application	Reference
Chemical engineering | Environment and Public Health	Wastewater treatment	New strategy to selectively separate pharmaceutical contaminants in wastewater deriving from hospitals	Cubis®-MSA-125P-100-DA-Semi-Micro Balance	Surfactant and ionic liquid mixing for characterization of binodal curves	5
Chemical engineering | Public Health	Wastewater treatment	Design of a biocompatible aqueous biphasic system to extract non-steroidal anti-inflammatory drugs from aqueous streams	Cubis®-MSA-125P-100-DA-Semi-Micro Balance	Concentration determination of binary mixtures	6
Chemical engineering | Biotechnology	Isolation of bio-technology-derived chemical products	Influence of electrolytes on liquid-liquid equilibria	Cubis®-Precision Balance	Water content determination, Karl-Fischer Titration	3
Chemical engineering | Chemistry	Aggregation behavior of ionic liquids in aqueous solutions	Implementation of alternative experimental techniques enables to understand better the aggregation behavior of ionic liquids in aqueous solutions	Cubis®-MSA-125P-100-DA-Semi-Micro Balance	Solution preparation for volumetric behavior and density determination	7
Chemical engineering | Environment	Replacement of non-biodegradable plastics with cassava biobased films (CBF)	Analysis of impact of novel cassava-assisted processing on fluid transport phenomenon in stressed bio-derived films	Cubis®-MSA-Analytical Balance	Film solubility and swelling ratio measurements	8

Field	Topic	Details	Type of Sartorius Cubis® Balance	Application	Reference
Chemical engineering | Biotechnology	Systematic investigation of salt-influence on aquerous | organic systems	Salt influence on MIBK | water liquid-liquid equilibrium: measuring and modeling with electrolyte Pertubed-Chain Statistical Associating Fluid Theory (ePC-SAFT) andthe thermo-dynamic model COSMO-RS	Cubis®-Precision Balance	Solution preparation for liquid-liquid equilibria measurements, Karl-Fischer Titration	25
Chemical engineering | Biotechnology	Solubility characterization of Aqueous Biphasic Systems (ABS)	Triton-X surfactants are proposed as candidates to form ABS	Cubis®-MSA-125P-100-DA-Semi-Micro Balance	Weight quantification to determine the ternary system compositions	26
Chemical engineering | Thermodynamics	Zinc-rich alloys, as new materials for latent heat storage application	New zinc-rich eutectic alloys, as phase change materials with melting temperature below 400°C and high energy densities are new materials for latent heat storage appliction	Cubis®-Precision Balance	Obtaining the stochiometric amounts of the primary metals	30

Discussion

From the fundamental to the state-of-the-art laboratories, samples are weighed multiple times each day. The present application guide presents a series of examples showing how laboratory balances are integrated into research workflows used in highly diverse and dynamic areas of sciences. The Sartorius Cubis® series of weighing systems fulfill the highest requirements at the level of accuracy and precision. These balances were designed for an intuitive operation, which is further aided by intelligent assistance systems which ensure the correct usage of the balance at all times. This ensures a higher degree of repeatability of the different workflows, while lowering the probability of human error during the measurement steps.

Abbreviations

ADME (Absorption, Distribution, Metabolism and Excretion)
SIMS (Secondary Ion Mass Spectrometry)
MALDI (Matrix-Assisted Laser Desorption Ionization)

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