

Summary

The preparation of demanding and/or toxic standard solutions in GLP/GMP- and FDA-regulated laboratory surroundings requires precise, absolutely safe and intelligent dosing systems. The Dosino, which has proven itself worldwide in the titration and sample preparation sectors, is ideally suited for such tasks. It guarantees fully documented working procedures and reproducible results. Its typical applications lie primarily in the fields of synthetic chemistry and sample preparation.

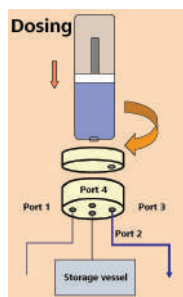
In synthetic chemistry, PC-based systems are increasingly being used for monitoring and controlling units. Typical liquid handling applications are the precise and safe dosing of aggressive and/or harmful solutions as a function of time, temperature, pH and other parameters. A further interesting Dosino application is the synthesis of metal-organic compounds in pilot plants.

Despite increasing possibilities for automation, sample preparation procedures are often still carried out manually. This is not only very labor-intensive, but also leads to errors. By the use of modern dosing systems in combination with modern Robotic Sample Processors, such sample preparation steps as pulverization, mixing, filtering, diluting and metering out can be reliably automated. In addition to the savings in time, the reproducibility and correctness of the analytical results are also improved.

Introduction

The Dosino technology applies the classical piston buret concept "upside down", i.e. the drive is located above the high-precision glass cylinder.

The advantages of this concept are: in case of a leak, the substances to be dosed out, some of which are aggressive, can no longer damage the drive. This arrangement is extremely compact and practical. The Dosing Units of the 800 Dosino can be mounted directly on bottles and canisters equipped with GL 45 screw heads. Adapters are available for the other types of threads. The ceramic disk located beneath the glass cylinder serves four freely definable ports for dosing functions. The glass cylinder can be emptied completely; the remaining dead volume is extremely low. The whole dosing procedure is not affected by air bubbles. The Dosino can also aspirate defined volumes of several solutions (and air), mix them, dilute them and dose them. This results in numerous possibilities for PC-controlled laboratory dosing, some of which are presented here.



Synthesis of metal-organic compounds

Preparative work with metal-organic compounds, which are extremely important in organic synthesis, is usually only possible in the absence of air, as they tend to react violently with moisture or oxygen. This means that the whole synthesis apparatus, including all connections to the Dosino, must be thoroughly purged with a protective gas after a previous check for leaks.



In the majority of applications, organo-magnesium and organo-lithium compounds and occasionally also silicon tetrachloride are added to carbonyl compounds. The dosing rates of the organo-metal compounds are in the range 0.1...2 mL/min; dosing times are from 2...5 hours.

In addition to its robustness, users value the flexibility and mobility of this dosing system, as it can be easily transported from one synthesis apparatus to the next. The Dosino excels by its precision, in particular at low dosing rates and in long-term dosing procedures involving small volumes; it is far superior to gravimetric dosing systems.

Preparation of standards

The preparation of calibration standards is a frequent source of error, particularly in shift work with changing personnel; this is usually caused by pipetting inaccuracy and insufficiently cleaned volumetric apparatus.

By using an automated dosing system consisting of 800 Dosino, 846 Dosing Interface and 840 Touch Control, individual errors are avoided by the user-independent preparation of the standards. In addition, contact with harmful substances is also reduced (1).



A sample assignment table ensures that samples with their own sample identification are automatically processed by the correct method. Repetitive identifications, such as occur in the preparation of external calibration standards, are saved in text templates and can be used again at a later date. For the preparation of a defined concentration of internal standard, automatic standard addition is carried out after previously weighing out the sample.

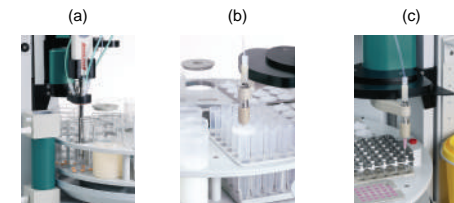
An individualized operator interface allows the amount of information that a window contains to be freely definable; this means that the user can only see the functions that are required. In order to increase the robustness of the system, the touch-sensitive control is used in preference to PC control.

Determination of pharmaceutical ingredients

In the determination of paracetamol, caffeine and propyphenazon in analgetics, the 800 Dosino can be used in combination with the 815 Robotic Filtration Soliprep as a sample preparation system for HPLC (2).



The tablets are automatically treated with eluent and then pulverized by a homogenizer. The resulting suspension is stirred for a few minutes before it is filtered through a disposable filter into a PP sample vessel or vial. The control of the dosing, filtering and sample changer operations, some of which are carried out in parallel, is by **tiamo™**, the laboratory automation and titration software.



- (a) left: tablets before eluent addition and pulverization
right: suspension, consisting of eluent and pulverized tablets
(b), (c): transfer within the rack and subsequent filtration of the suspension through disposable filters into PP sample vessels (b) or vials (c)

Further applications of the various Soliprep systems cover the determination of water and benzbromaron in tablets, the determination of the CTAB surface (adsorption of N-cetyl-N,N,N-trimethyl ammonium bromide) of silica gels or soot and many more.

Summary

The 800 Dosino controlled by **tiamo™** (parallel operation) or Touch Control (single or tandem operation) can be used universally for dosing and liquid handling tasks in both the analytical laboratory or directly in the synthesis laboratory.

References

- (1) E. van der Heijden and A. Steinbach, Automated preparation of surrogate mixtures for the determination of octane and cetane numbers, Pittcon 2008, <http://products.metrohm.com> (search for 8.000.6022EN).
- (2) E. van der Heijden and P. Krebs, Probenvorbereitung im analytisch-chemischen Labor, GIT Labor-Fachzeitschrift 52, 11-13 (2008).