

# Pharmaceuticals in Review

## Middle-European Pharmaceuticals in a Changing World

Heinz Sucker



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**W**hat has been the Middle-European contribution to pharmaceutical evolution in the past 25 years since *Pharmaceutical Technology* was established?

### Roots of European involvement

The circumstances of the second World War caused pharmaceutical technology to grow slowly from the former art, *ars pharmaceutica*, also associated with the name *galenics*. The impetus for this growth first came from Switzerland, especially by the well-known book, *Galenisches Praktikum*, by K. Münzel and

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J. Büchi in 1959 as well as articles from K. Steiger-Trippi. For young Germans, S.H. Schou (DK) and E. Sandell (S) from Scandinavia have been exemplary. In the United States, T. Higuchi initiated physical pharmacy that was introduced mostly by the famous textbook, *Physical Pharmacy*, by A.N. Martin, J. Swarbrick and A. Cammarata in 1960.

The most important areas of progress and the most difficult challenges of the pharmaceutical sciences have been biopharmaceutics and chronopharmacology, both of which began in Europe. The roots of biopharmaceutics resulted from the research by L. Michaelis and M.J. Menten (1913), E. Widmark and J. Tandberg (1924), T. Theorell (1937), and finally the initiator of pharmacokinetics, F.H. Dost (1953) as well as E. Krüger-Thiemer in 1960. Chronopharmacology first was mentioned by J. Aschoff and F. Halberg in the early 1960s. In the United States both fields grew to full bloom. The former was developed by Riegelmann, Nelson, Wagner, Garrett, Levi, Gibaldi, and Benet, and by Rowland in the United Kingdom. The latter was of great importance for medicine in space flight.

### Problem areas

During the past 25 years, the key issues in drug dosage form development were dissolution rate, content uniformity, bioavailability, bioequivalence, compatibility, stability, scale-up, quality assurance, in-process control (IPC), good manufacturing practices (GMPs), microbiological purity, oral and intramuscular controlled-release formulation, and absorption of problematic drug substances, e.g., ciclosporin (cyclosporine, USP). The scientific range of pharmaceutical technology had to be broadened, e.g., the use of statistical methods for IPC, the skill to adapt all equipment and processes according to the microbiological requirements in GMPs, to make use of modern, highly sensitive analytical methods in pharmacokinetics, and to carry out and evaluate clinical test in humans and animals.

### European contributions

German-speaking personnel in pharmaceutical technology are characterized by their close connection to mechanical engineering and the good cooperation among academic research, practical development at the bench, and scale-up in production as well as with manufacturers of excipients and process equipment.

Examples of excipients for specific pharmaceutical use and/or grade from European manufacturers are colloidal silicon di-

oxide, silicium dioxide (Degussa) povidone and derivatives, polyvinylpyrrolidone (BASF), polymethacrylates, acrylic polymers (Röhm GmbH), polylactides and polylactide-co-glycolides, lactic and glycolic acid polymers (Boehringer Ingelheim Chemicals), and hydroxypropyl- $\beta$ -cyclodextrin (Janssen). Also, the Swiss Catalog of Pharmaceutical Excipients (1974) was the basis for the *APhA Handbook of Pharmaceutical Excipients* (1986).

Pharmaceutical processes developed in Europe are (to name a few) fluid-bed drying, granulation and coating (Glatt, Aeromatic, Hüttlin), roller compaction (Alexanderwerk, Gerteis), laboratory-scale equipment (ERWEKA), packaging technology involving blister-strip packs (e.g., Harro Höfliger, Klöckner, Seidenader), the sterile multidose nasal sprayer (Pfeiffer), and the bottle-pack aseptic system (rommeLag).

Cooperation between industry and university labs led to the development of special test methods such as the instrumentation of tablet machines, the very early introduction of statistical methods in IPC and closed-loop process controls, the determination by power measurement of the liquid requirement for a conventional granulation process, and the automatic drying of pharmaceutical granulates in the fluid bed.

This tight cooperation also can be witnessed in fluid career transitions — researchers have been known to become scientific managers and successful industrial managers have become academic chairpersons.

### The future

New professors, in continental Europe at least, are much more concerned with matters of primary biological emphasis such as cell cultures, Caco cells, vectors for cancer therapy or gene transfer systems, and biocomputers. Whether the results of their research will culminate in marketed dosage forms, however, is open to question. Somewhat unsurprisingly, the number of younger faculty members without a background in pharmaceuticals is increasing.

In industry, the importance of pharmaceutical development and technology is decreasing. Analytical departments have become independent profit centers, concentrating less on research and more on rapid development. The new belief is that everything can be bought easily. The topics of current interest include qualification, validation, documentation, standard operating procedures, and cleaning. These areas, although important, were formerly self-evident — not part of research.

For PhD students, areas such as medical advice and pharmaceutical care have overtaken the manufacture and analysis of dosage forms as essential areas of interest. These developments will no doubt echo in the United States as pharmaceutical development and technology will be downgraded further in favor of clinical pharmacy.

What about *Pharmaceutical Technology*? It must continue to maintain the balance of the academia-industry-authority triangle to provide a respected forum where these three can meet and discuss, openly and without prejudice, the obstacles that might prevent the development of better drugs and dosage forms in the future. **PT**