

Efficient drug research and development with the Freedom EVO[®] 75

Toa Eiyo in Japan is a pharmaceutical company specializing in the research and development of pharmaceutically unique medicinal products for cardiovascular diseases such as angina or heart attacks. The Company's pharmacokinetic testing laboratory in Fukushima has chosen the Freedom EVO 75 equipped with an 8 Plus 1 Access[™] Liquid Handling Arm to achieve greater efficiency by automating its sample preparation steps.

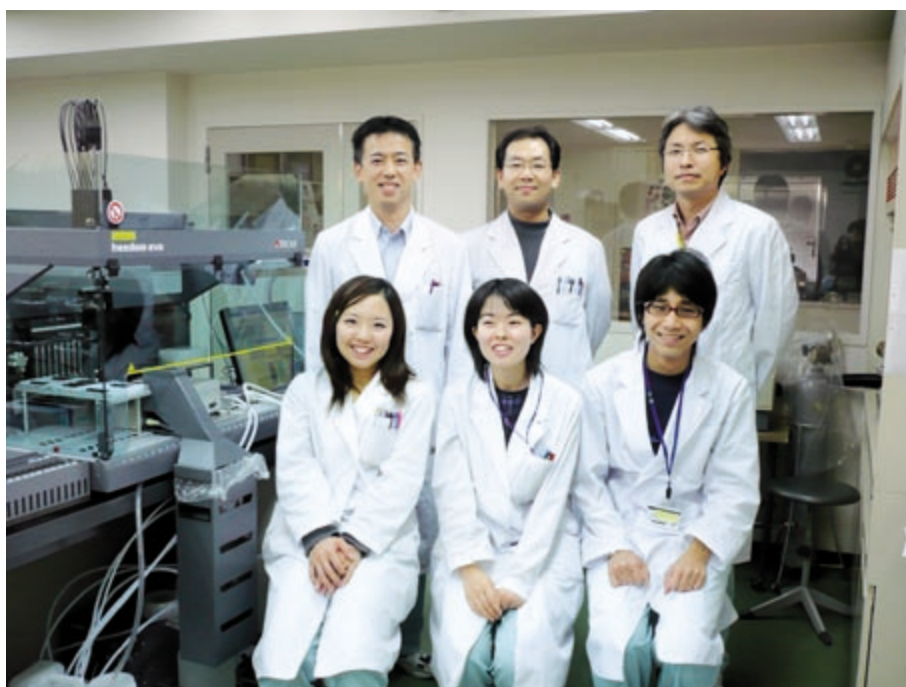
The development of new drugs at Toa Eiyo starts with the synthesis and evaluation of various novel low molecular weight compounds at its Tokyo Research Laboratories. The compounds that demonstrate potency are selected for pharmacokinetic testing at Toa Eiyo's Fukushima Research Laboratories. Mr Yoshiaki Watanabe, chief scientist, explained: "Preliminary pharmacokinetic studies using cells of human origin or artificial membranes are performed at our Tokyo Research Laboratories, and promising compounds are transferred to our section for further pharmacokinetic, toxicity and safety testing. Our section has around 20 members, of whom six are involved in pharmacokinetic studies, involving measurement of drug concentration in blood plasma from animal testing and clinical trials. In addition, Toa Eiyo's Pharmaceutical Technology Center is making special efforts to develop drug formulations that are pharmaceutically unique, and pharmacokinetic profiles of

these new formulations are also evaluated in our section. With this recent increase in the number of samples we analyze, we wanted to automate the sample preparation steps to achieve greater efficiency. Tecan's liquid handling devices greatly attracted our interest at the 8th International ISSX Meeting in October 2007, and we selected the Freedom EVO 75 with integrated 8 Plus 1 Access Liquid Handling Arm, which offered the management of pipetting precision with its liquid level detection system."

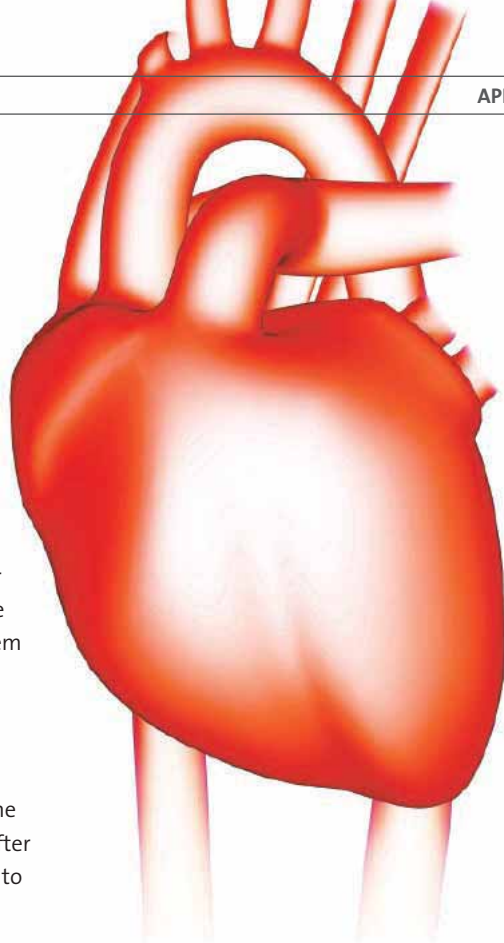
They use the Tecan instruments for automated preparation of blood plasma samples, which involves solid phase extraction (SPE) or deproteinization in 96-well filter plates, using customized programs for each step. As pipetting precision is critical, an integrated balance is used before each run to confirm the pipetting precision of the first channel, which is used for sample transfers, while all eight channels are used for other preparation tasks. Mr Watanabe



Toa Eiyo's Pharmaceutical Technology Center develops pharmaceutically unique formulations for the treatment of heart disease.
Photo provided courtesy of Toa Eiyo



Toa Eiyo's pharmacokinetic team (l to r, back row): Mr Yoshiaki Watanabe, Mr Kazuhiro Taniyama, Mr Takashi Sato (l to r, front row) Ms Sakiko Suzuki, Ms Marie Tanaka, Mr Toshihisa Kodama



is considering this step as a useful test for compliance with Good Laboratory Practice standards. The Liquid level detection system on the first channel helps to prevent sampling error and minimize wastage of valuable samples, further enhancing pipetting reliability. Just by setting blood plasma samples in the Freedom EVO 75, the preparation is completed automatically, after which the samples are simply transferred to the LC-MS/MS for analysis.

“The automated preparation of one plate with 96 plasma samples takes an hour and a half to two hours whereas, by manual pipetting, it used to take at least half a day,” Mr Watanabe elaborated. “The preparation stage is no longer a bottleneck, because the automated process is faster than the LC-MS/MS analysis. The Freedom EVO 75 could process four or five plates in a day but, with the current set-up, we process two or three plates in a day and analyze the samples overnight on multiple LC-MS/MS systems for the results to be collected the next morning.”

Another objective of introducing the automated aliquoting device was to prevent human error. Mr Watanabe continued: “Until recently, we have been handling a large number of samples manually, paying a great deal of attention to minimize mistakes but, by automation, that kind of human error can now be prevented. Automation has also removed the psychological burden on the researchers; with a small number of people participating in a wide variety of tasks, automation can create more space in the scientists’ time, and we anticipate that we will be better able to plan our research themes. We have already seen savings in time, and the amount of precious samples used.”

“The characteristics of the Freedom EVO make it easy to use for many researchers. Even without specialist knowledge, it is very easy to write a script in Freedom EVOware®, and it is possible to adapt existing programs for other manipulations with just a few changes.”

Mr Watanabe is planning to use the Freedom EVO 75 in other projects: “We would also like to apply our workflow to other pre-clinical tests, to evaluate numerous evaluation compounds efficiently, like solubility screening, metabolic stability testing, etc. These are currently being carried out manually, but we would like to automate as many of the routine tasks as possible.”

“For the efficient progress of research projects, it becomes critical that each research worker can make decisions based on the data obtained, and the installation of an automated pipetting device that can be applied to pre-clinical and clinical tests has been very welcome. It has already helped to reduce the burden of routine manual tasks, and we anticipate a far-reaching effect of its use in our future research themes,” concluded Mr Watanabe.

First established in 1943, Toa Eiyo has always been a research and development oriented corporation, utilizing the vitamin B2 contained in silkworm pupae to become the top manufacturer of vitamin B2 formulations in Japan. In the 1980s, Toa Eiyo successfully developed heart disease treatments, which were immediately praised by many in the medical field as unique and effective products. Today, Toa Eiyo specializes in the development of drugs for use in the treatment of circulatory and cardiovascular conditions such as ischemic heart disease, including angina and myocardial infarction, and is dedicated to supporting and enhancing the quality of life of patients.

Many now look to the company to deliver hope to patients with heart disease. Toa Eiyo is committed to pursue ever higher levels of original research and development at its facilities, aiming to become a leading specialized pharmaceutical company with a truly valued role in the field of circulatory and cardiovascular treatment. The demand for better and safer medicines to treat adult-related diseases will continue to increase, and Toa Eiyo is responding to the needs of the approaching ‘era of the elderly’ as its most important social objective.