Dissolved oxygen quantification in oxygen sensitive products

Study of DO values at laboratory and industrial scale-up

Industry: ChemPharma API
Application: DO measurement in API production
Hamilton products: VisiPro DO Ex; ODO Cap H2, immersion fitting (HCP)

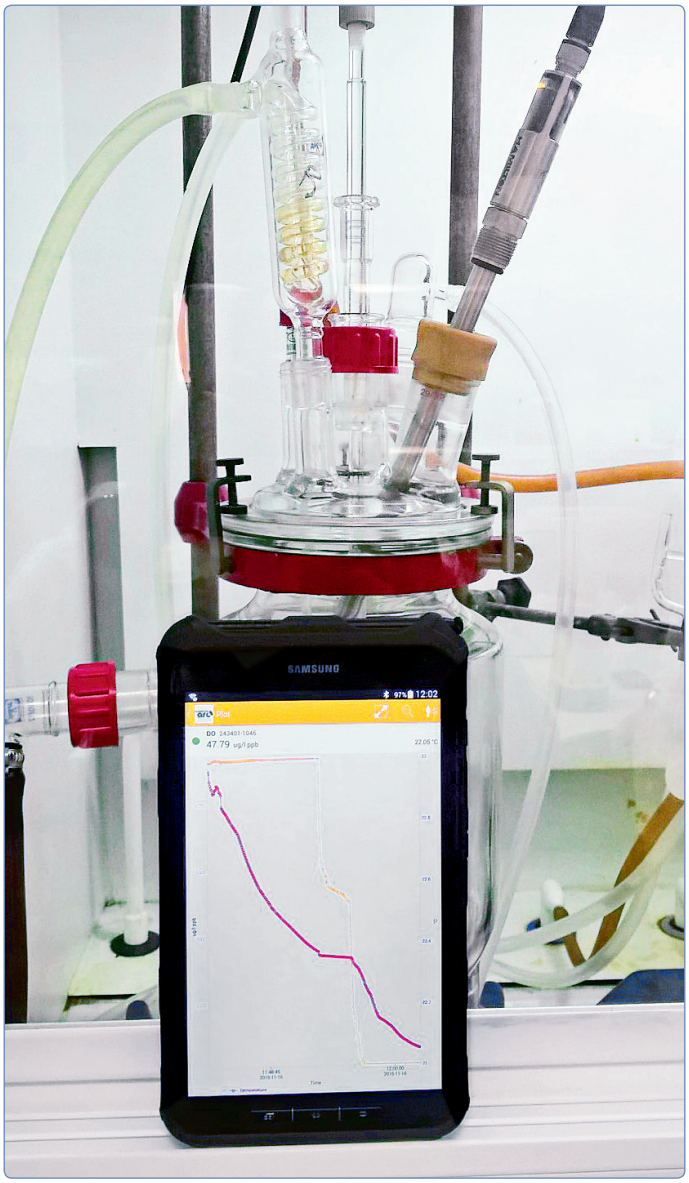

Fig. 1: Set-up for the laboratory tests

Sulfur is an essential component of all living cells as it is contained in the amino acids cysteine and methionine and so the element is present in all polypeptides, proteins and enzymes that comprise these amino acids.

Sulfur containing compounds often show biological activity and for this reason are found in multiple drugs. Sulfonamides, thioethers and sulfones are the most common functional groups in sulfur containing drugs although other sulfur containing moieties such as thiophenes and thiazoles can be found in pharmaceutical molecules as well. For example, sulfonamides are found in diuretic or hypertensive drugs, and the main function of sulfones which are present in numerous medicines is to act as pump inhibitors. Sulfonamides were the first antibiotics to be used systemically and paved the way for the antibiotic revolution in medicine. Sulfur is also present in penicillin which was the first medication to be effective against many bacterial infections caused by staphylococcus and streptococcus species. Penicillins are still widely used today, though many types of bacteria have developed resistance following extensive use.

Medichem is an Active Pharmaceutical Ingredient (API) and Finished Dosage Form (FDF) developer and manufacturer with headquarters in Barcelona (Spain) and manufacturing sites in Girona (Spain), Malta and China. Due to its long history in the pharmaceutical industry, Medichem has developed an extensive portfolio of APIs covering more than 15 therapeutic areas. Some of these APIs include sulfur containing compounds and were developed many years ago but during the last years there was a need to adapt these old processes to fulfill Medichem's continuous commitment to quality and environmental sustainability.

The main problem that chemists face when working with some functional groups containing sulfur is the risk of oxidation of the sulfur moiety when atmospheric oxygen is present and this represents an additional challenge to any process and a parameter to take into account. To avoid oxidation new technologies can be extremely useful, for example the dissolved oxygen sensor (DO). Medichem contacted Hamilton in order to find a solution for monitoring and controlling oxygen levels in one process. The VisiPro DO Ex sensor

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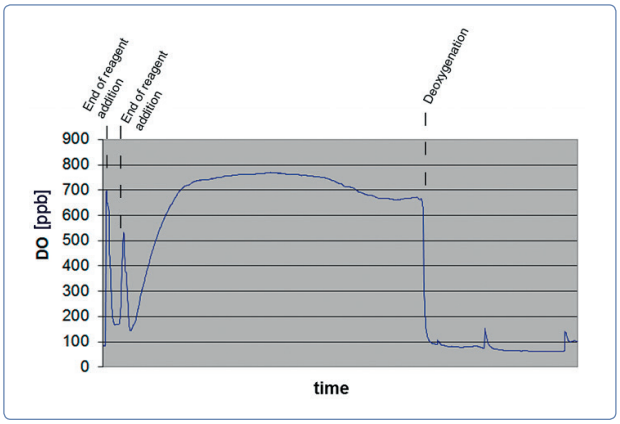
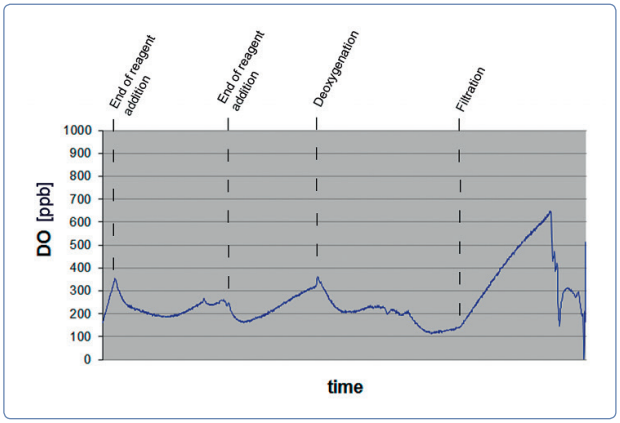
BENEFITS
VisiPro DO Ex

- Optical sensor technology
- Quick and easy maintenance
- Stable and reliable readings in acidic and basic media system
- Intelligent sensor technology
- Bluetooth 4.0 to monitor data on mobile devices



Graph 1



Graph 2

provided by Hamilton met all the expectations and allowed to produce product with a high quality avoiding undesired by-products. The VisiPro DO EX is suitable for laboratory use as well as for pilot plant scale and it is very sensitive achieving detection levels of ppbs. Moreover, the sensor has to be able to compensate media changes as the reaction proceeds, making it possible to monitor and collect data during the whole process.

Same sensor for laboratory and pilot plant scale

At laboratory scale, while developing and polishing the final process conditions the sensor was connected to a laptop via Bluetooth. All data received from the sensor was collected and stored in an excel file for subsequent study. At pilot plant scale, the main issue was to comply with ATEX Zone 1 requirements. The sensor was mounted in a PVDF immersion fitting supplied by Hamilton and customized to Medichem's requirements. Its 4-20mA 2-wire signal output was directly connected to the process control system.

Getting the complete chemical reaction profile was very important because it allowed identifying critical points where oxygen levels increased drastically (charge of reagents, aging, filtration, drying etc.) and implementing corrective actions to minimize its effect. As shown in the graph 1 below, under normal reaction conditions and no de-oxygenation, DO levels were very high (800 ppb). After studying the full reaction profile using VisiPro DO Ex and once the corrective actions were made, DO levels decreased considerably (300 ppb, graph 2). At laboratory and pilot plant scale, VisiPro DO Ex showed the same performance. Both reaction profiles matched perfectly and no discordance was observed during scale up.

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REF 695218/01 — 03/2017

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