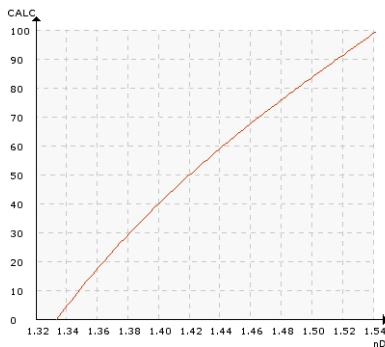


SUCROSE DENSITY

Typical end products

Viral vaccines e.g. seasonal influenza, meningitis, rabies, hepatitis B, polio, measles, mumps, rubella and other vaccines

Chemical curve: R.I. per BRIX at Ref. Temp. of 20°C



Introduction

The viral vaccines are either produced by inoculating viruses into specific pathogen-free eggs or in animal cell culture based process. The allantoic fluid of these processes is harvested and purified by centrifugation and stabilised with buffer containing sucrose.

The continuous flow ultracentrifugation technique is typically used for producing purified and concentrated virus particles on a large scale. The internal subviral core of the virus is separated and fractionated on the basis of their sedimentation rate and the buoyant sucrose density.

The K-Patents Pharma Refractometer PR-23-AC is used for accurate measurements of these sucrose densities.

Application

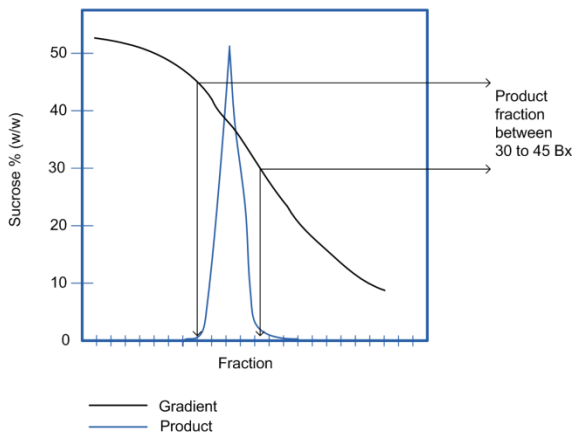
The ultracentrifuge contains six flow channels that process material flows during the operation. The different process steps are as follows:

1. The density gradient is loaded into the rotor. A sucrose gradient may consist of layers decreasing from 70% sucrose to 20% sucrose in 10% increments.
2. As the rotor is gradually accelerated, the gradient reorients itself vertically along the outer rotor wall.
3. Sample fluid is pumped into the rotor on a continuous flow basis.
4. The sample particles sediment radially into the gradient of increasing density. They eventually band (iso-pycnally) in cylindrical zones where the gradient density equals a particle's buoyant density.
5. At the end of the run, the rotor is decelerated to rest. The gradient reorients itself to the original position without disturbing the particle bands.
6. The banded particles are now ready to be unloaded. Fractions are collected using a small peristaltic pump or air pressure according to the sucrose density gradients measured by K-Patents Process Refractometer.

Installation

The K-Patents Pharma Refractometer PR-23-AC can be installed in the vaccines fractionation unit for in-line process control. The output of the transmitter is a 4 to 20mA DC output signal proportional to sucrose solution density, concentration, Brix or other scale that has been selected for the instrument.

Collection of the virus rich fraction



The measurement signal is used for reliable and timely determination of the product peak in the density gradient (0 to 60% w/w sucrose), the subsequent collection of the virus rich fraction (Figure) and in diverting the virus rich fraction in the correct container.

Another key area of the PR-23-AC application is in the research and development phase when the researchers need to develop a process understanding and to characterize the concentration (or density) of sucrose in each fraction. This information is valuable when formulating banding patterns and optimizing the target fraction. Once the operating procedure has been developed, the refractometer is required at the full scale production for determining the moment when to begin and to stop collecting the target fraction.

The typical system comprises of a Pharma Refractometer PR-23-AC unit and a Pharma Mini Flow Cell PMFC-HSS that allows the sensor connection to the zone ultracentrifuge rotor unloading and fractionation phase. The standard Ethernet communication solution allows for simultaneous data logging and continuous monitoring of the measurement values and diagnostic data from an Indicating transmitter DTR to a computer via an Ethernet connection.

The optional Field Communication software program CC-11 provides further communication features such as drawing and monitoring of real-time trend chart on the computer screen, saving the measurement data in PDF format and saving and storing the batch data over a selected period of time.

Instrumentation



Description

K-Patents Pharma Refractometer PR-23-AC with Pharma Miniflow cell PMFC-HSS for installations with small sample volumes and 5 mm inlet and outlet clamp connections. Miniflow cell is installed to the sensor through a 3A Sanitary clamp.

Measurement range:

Refractive Index (nD) 1.3200 – 1.5300, corresponding to 0-100 Brix.