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Historical Review on Centrifuge Device, Function, Design and improvement strategies

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Abstract

This paper presents facts and figures related to medical centrifuges and reviews various historical aspects, directly or indirectly, concerned with medical equipment reliability including classifications of centrifuge, function, design and other professionals to improve centrifuge reliability. A number of error was careful considered in aspect of design consideration. Centrifugation separates particles within the specimen according to their shape, dimensions, and density and basically can be defined as a separation method. The centrifuge is an essential device in medical laboratories to prepare the serum, plasma, and urine samples for analysis.

Keyword: Centrifuge; Historical; Design; function

I Introduction

A centrifuge is a laboratory device that is used for the separation of fluids, gas or liquid, based on density. Separation is achieved by spinning a vessel containing material at high speed; the centrifugal force pushes heavier materials to the outside of the vessel. [1] This apparatus is found in most laboratories from academic to clinical to research and used to purify cells, subcellular organelles, viruses, proteins, and nucleic acids. There are multiple types of centrifuge, which can be classified by intended use or by rotor design. From the large floor variety to the micro-centrifuge, there are many varieties available for the researcher. Centrifugation basically can be defined as a separation method. It separates particles within the specimen according to their shape, size, and density by the centrifugal force obtained from the rotation [2]. The centrifuge is a device developed for the separation of mixtures consequently, it is commonly used in medical laboratories to prepare the serum, plasma, and urine samples for analysis. An accurate and precise centrifugation process (pre-centrifugation phase, centrifugation phase, and post-centrifugation phase) is essential to defeating errors in the preanalytical phase.[3] The purpose of this paper is to ensure the standardization of a good, precise protocol for the centrifugation process among the medical laboratories.

II. Historical Review

As one of the most commonly used laboratory instruments today, the centrifuge offers an efficient means of preparing and separating samples of different densities often for scientific and medical use.[4] This form of density-driven preparation has been around for centuries, dating as early as the 1400s with simple hand-powered milk separators, however a formal commercialized version of the centrifuge did not emerge until the 1800s. In 1864, Antonin Prandtl invented the first centrifuge-type machine, which was used in the dairy industry to separate milk and cream on a large scale. Following Prandtl, Friedrich Miescher, a Swiss physician and biologist, was the first to apply centrifugation in the lab. From a crude centrifuge system, he developed in 1869, Miescher was able to successfully isolate nucleic acids from the nuclei of white blood cells, which served as an important development in the discovery of DNA inheritance. Miescher's work quickly attracted attention in the field, leading to the swift development of the first continuous centrifugal separator in 1879 by Gustaf de Laval, originally introduced as an impulse steam turbine. De Laval's concepts allowed for the ultimate commercialization of the centrifuge and have been used to develop modern rocket engines and dairy industrial equipment. The next evolution of the centrifuge occurred in the 1920s with the development of the ultracentrifuge by Swedish chemist Theodor Svedberg. This new ultracentrifuge could reach 900,000 g, while other routine models at the time were only capable of reaching 260,000 g. This enabled Svedberg to determine the molecular weight and subunit structure of highly complex proteins and viruses, which revolutionized the study of protein structures. Svedberg received the Nobel Prize in chemistry in 1926 for his invention of the ultracentrifuge. While Svedberg's design allowed much advancement, his ultracentrifuge functioned strictly as an analytical instrument, ultimately preventing its use as a preparative device due to its horizontal rotor axis. The research of French physicist Emile Henriot, however, enabled this transition. Henriot's independent work consisted of using compressed air to generate high velocities, translating to high rotational speeds for centrifugation. By the early 1930s, biologist Martin Behrens was using the centrifuge to isolate cell structures. Alongside Behrens' work was that by biologists Robert Bensley and Normand Hoerr, who could reliably produce a mitochondrial fraction by 1934. With the work of these three scientists, the technique of true cell fractionation via the centrifuge could be achieved and later refined.

Meanwhile, Jesse Beams of the University of Virginia started developing a centrifuge for isotopic separation in 1934, including vacuum design. Beams' graduate student Edward Pickels continued refining this vacuum centrifuge to create the first high-speed model in 1938 with Johannes Bauer in an attempt to isolate and filter viruses. Pickels also went on to create the first electrically-driven vacuum centrifuge in 1942, after which Pickels cofounded Spinco, where he marketed a truly preparative device capable of reaching speeds up to 40,000 rotations per minute in 1949. Throughout the beginning of this time, Beams worked on the Manhattan Project to isolate uranium isotope U-235 through the use of a gas centrifuge, but his design was deemed inadequate to produce enough highly enriched uranium for the timeline of the atomic bomb project. With growing international focus on uranium production, the Russian nuclear weapons program set prisoner of war Austrian physicist Gernot Zippe on the centrifuge task. By the early 1950s, Zippe, with the help of fellow Austrian POW Max Steenbeck, had streamlined Beams' design for stable and reliable production. Amazingly, Zippe and his colleagues were paid and released from the USSR in 1956 to commercialize the centrifuge.

In the United States, 1954 brought vast improvements to the commercial centrifuge when Beckman Instruments (now Beckman Coulter) bought out Spinco, creating instruments with new high speed motors and better rotors. Meanwhile, Myron Brakke, a plant virologist working at the Brooklyn Botanical Garden, developed density gradient centrifugation, which provided more reproducible results for tissue fractionation than previous methods.
Zippe made his way to the University of Virginia in 1958 to show how to make efficient gas centrifuges. The US made this gas centrifuge research classified in 1960; all the while, scientists in Europe could continue freely pursuing it. Zippe went on to help start Urenco, which uses gas centrifuges to process uranium for nuclear power.

In 1962, the German company Netheler & Hinz Medizintechnik (now known as Eppendorf) created the first microcentrifuge for lab use. This microliter system was subsequently developed by various other labware and biotech companies, ultimately giving birth to the centrifuge's prevalence within lab environments today.

The first microprocessor-controlled centrifuge was introduced in 1976, innovation that was years ahead of its time, at ACHEMA by Hettich. Then Beckman launched floor ultracentrifuges in the

1980s, and Eppendorf launched personal centrifuges in 2000. And centrifuge technology has continued to improve commercially ever since, now used for density separation (as originally developed), isotope separation, aeronautics and astronautics, and geotechnical simulations. With prominent medical and biotech use, especially concerning protein and nucleic matter research, the centrifuge will no doubt continue to evolve and prove essential within the lab.

III Classification of Laboratory Centrifuges

A. Divided by structure:

i. Desktop centrifuge: This desktop centrifuge is ideal for spinning down 50 mL samples in breweries and wineries. Ruggedly built, the centrifuge attaches solidly to your bench with suction cups, and offers programmable speeds and times. Centrifuges up to six 50 mL samples simultaneously. With following specification Speed: 4,000 RPM, Capacity: 6 x 50 mL tubes, Voltage: Varies by model

ii. Floor-standing centrifuge: Floor standing centrifuges are designed for the centrifugation of large volumes, or for very high speeds. **floor standing centrifuges** are designed for holders of large sample containers. They are Ideal for use in routine clinical diagnostics, clinical laboratories, blood banks and pharmaceutical laboratories. A high performance and comprehensive range of accessories ensure centrifugation runs are quick and reliable. The floor standing centrifuges are excellent for large volume samples, but also because they have a wide range of accessories for blood collection vessels, centrifuge tubes, bottles and different blood bag systems can all be used with one rotor; it is not necessary to change the rotor. Low noise emissions contribute to a safe and ergonomic pleasant working environment for all lab personnel.

B. Divided by speed: low speed centrifuge and high speed centrifuge.

i. **Low speed centrifuge**: A separation method where the components of a sample are separated on the basis of their density in a centrifuge according to the centrifugal force they experience. Samples are spun at <5000 rpm.

ii. **High speed centrifuge**: A High Speed Centrifuge is a device that uses centrifugal force to separate particles of different mass or densities suspended in a liquid. Rotating the solution in the tube at high speeds gives the angular momentum of each particle a centrifugal force proportional to its mass.

C. It can be divided according to temperature control: refrigerated centrifuge (low temperature centrifuge) and normal temperature centrifuge.

i. Low temperature centrifuge: Refrigerated centrifuges have been developed to help minimize the effects of temperature on several analytes, including many temperature-sensitive enzymes and hormones. Laboratories should include the required centrifugation temperatures in their sample handling operating procedures.

ii. Normal temperature: Most of the work in a refrigerated centrifuge is done at 4 °C. Most centrifuges will claim a lower temperature range of –20 °C, but not all. The rating may pertain to all conditions, or it may be the result of a single rotor being tested in a 70 °C lab in low humidity,

IV Function of Centrifuge

1. To separate cellular and subcellular components
2. To Separating one cell type from another.
3. Removing cells or other suspended particles from their surrounding milieu on either a batch or a continuous-flow basis.
4. To Isolating viruses and macromolecules, including DNA, RNA, proteins, and lipids or establishing physical parameters of these particles from their observed behavior during centrifugation.
5. To study the effects of centrifugal forces on cells, developing embryos, and protozoa. These techniques have allowed scientists to determine certain properties about cells, including surface tension, relative viscosity of the cytoplasm, and the spatial and functional interrelationship of cell organelles when redistributed in intact cells.

V Centrifuge Design

To separate fluids, the centrifuge spins samples at a fast rate, resulting in heavy components to migrate away from the center axis and lighter components to migrate towards the axis. Centrifuge devices are widely used tools in food processing and medical research for cellular, genetic and protein analysis. When designing laboratory and medical centrifuges, several design challenges must be considered.

Many samples, such as live cells, tissues and proteins, are temperature sensitive. They must be stored and tested at precise temperatures to ensure proper reaction and viability. Additional design challenges include reduced footprints, noise levels, vibration and power consumption. In addition, many governments have restricted the use of traditional and natural refrigerants central to compressor-based systems.

To ensure precise temperature control for laboratory and medical centrifuge applications, active thermoelectric coolers and assemblies are more advantageous solutions for centrifuges compared to compressor-based systems. Peltier-based thermal management systems deliver stable and reliable performance at a lower total cost-of ownership

The basic operation principle of the centrifuge designed is the sedimentation principle in which the rotator accelerates the centrifugal force to separate the heavy particles in the samples. This allows for separation of different reagents at different speeds to gives the result instantly. The centrifuge is constructed in such a way that it has a switch which controls it's on and off, a speed control which determines the relative centrifuge force (RCF), the rotor which bears the centrifuge buckets, the bucket in which the centrifugation tubes are placed.

VI Materials

The design, material selection and development of the centrifuge were based on the following concepts and considerations: 80mm thick mild steel U-channel was used to fabricate the centrifuge frame in order to withstand vibrations that may arise from its operation. The centrifuge comprises of two aspects which includes

i. Mechanical Aspect

ii. ii. Electrical Aspect

VII Future improvement of centrifuge

After many years of research into the alternative possible methods for enriching uranium, it now appears that each of the major players have reached a common conclusion, that high speed gas centrifuges hold the key to the future.Alongside the recent announcements that the atomic laser enrichment programmes are being brought to a halt, there have been new proposals to revive the development of the gas centrifuge. [6] Urenco have had a continuous development programme for more than 30 years and now have a lead cascade of the latest generation of machines in operation (their sixth generation).

To expand this further, as have noted above, in the past, Urenco has always taken a well-considered and step by step approach to developing each centrifuge generation. They have set out the development programme in three stages: R&D, Qualification and Production Demonstration.

1. R&D: This includes all the theoretical and design studies, testing of all new materials, manufacture and spin testing of a small number of components, and building and testing of typically 10 or 20 centrifuges.

2. Qualification: The qualification phase is employed to prove that the centrifuges will operate successfully long term under all plant design conditions. Manufacturing routes have to be established and proven by the production of typically 100 to 200 centrifuges.

3. Production Demonstration: This involves the increase in manufacturing rates from the small demonstration levels needed for qualification, to the full production requirement of several thousand per year. This culminates in the building and operation of a lead cascade; or demonstration cascade, in which all the final designs and modifications are brought together. Where the need for modifications is identified, these will all be tested and backed up by appropriate theoretical studies, so that the lead cascade has the best possible chance of successful operation. Only after a period of around 6 months, operation of the lead

cascade, would a decision be taken that the new generation is successful and should then be adopted for production use.

Generally, the overall programme has taken 7 to 8 years; 2 to 3 years for R&D, 2 to 3 years for qualification, and 2 years for production demonstration.

However, as we have reached the latest generations, the programme timescale has become more and more difficult to maintain. In the past, as and when the latest machine has been demonstrated successfully, it has been introduced at the earliest opportunity as a step change. This has always carried risks, in that the change over can bring "teething problems" where the new manufacturing route takes longer to effect than had been planned, or throws up one or two new problems in the ability to meet the stringent specifications, that were not so obvious in the demonstration phase. Again, in the past, when our expansion programme gave time for an occasional pause to ensure that the new generation was brought in successfully, there was time to resolve the teething troubles. Given the need to maintain an ongoing plant construction programme over the next few years, this policy will be modified, in that the switch to TC21 from TC12 will be phased, with a period when both types of machine will be in production, with the TC12 initially taking the production lead, but, as experience is gained, production of TC21 will increase and TC12 phased out, perhaps over a 3 year period.

The philosophy in the Urenco Group to R&D in the past has always been to carefully develop through testing of new materials, to manufacture and testing of individual components, through to successively running single machines, then demonstration cascades. This has given the successful introduction of each new generation, with only limited risk – the technical performance has been known, prior to making the decision to step forward. As the generations have been introduced, the technical difficulty and need to push the design closer to its operating limits have become greater, and it is now clear to Urenco that the latest generation centrifuge, the TC21, is the last in the family which started in the 1970's. The TC21 has now been operating for more than 15 months in a lead cascade, and is operating very successfully. If this performance continues, and when the economics of manufacture have been confirmed, Urenco will be taking a decision within the next 18 months for a phased introduction of the TC21 in our production plants. Further generations of centrifuge would be possible, but would probably

take more than the 7 to 10 years which Urenco has achieved in the past, and would lead to plants that would be less flexible in operation. With such a mature technology, Urenco is now following an R&D philosophy that will focus on improvements to the latest generation of centrifuge, the TC21, which will enable a series of improvements to be put into production use, as and when they are proven. In this way, Urenco is confident of maintaining its current position as the operator of the most advanced and lowest cost technology, well into the future.

Conclusion

The centrifugation is a modern & easy technique of separation and sedimentation on the basis of shape, size and density of macromolecules and other particles. In the centrifugation there are different types of forces are applied like as centrifugal force, gravitational force and centripedal force etc. and also different types of rotors are to be used that is; Swinging Bucket Rotor and fixed angle rotors at different RPM/RCF.

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