Review of cascade refrigeration systems for vaccine storage

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Abstract: Various models are already developed to achieve the refrigerating effect. Each refrigeration system has its own set of benefits and drawbacks, as well as a unique application. The vapor compression refrigeration system and the sorption refrigeration system are the two most prominent refrigeration technologies that may be utilized for a variety of purposes. In the medical profession, cascade refrigeration will be established in the storage of blood banks, plasma, vaccines, bone banks, biological fluids storage, etc. Storing heat-sensitive vaccines at the right temperature is crucial yet often difficult by the availability of ultralow temperature cold storage. This paper has reviewed that the different types of cascade refrigeration systems for a better refrigerating effect on vaccine storage.

1. Introduction
Cascade system is a low-temperature refrigeration technology that is utilized for ultra-low cold temperatures (-40°C to -130°C). Simple Vapour Compression Refrigeration Cycle (VCRS) is ineffective at such ultra-low temperatures owing to an influential compression ratio, which leads to significant discharge issues and low volumetric efficiency. However, cascade system is significantly more efficient in such settings. The cascade refrigeration cycle is typically a blend of two VCRS cycles, known as low temperature circuit (LTC) and high-temperature circuit (HTC), which are used in conjunction with a cascade condenser. This cascade condenser serves as that of an evaporator for LTC and then a condenser for a HTC. The low-temperature circuit uses low-boiling refrigerants, whereas the high-temperature circuit uses refrigerants having high boiling points.

1.1. Principle of Cascade Refrigeration Technology:
To condense refrigerants which can attain ultra-low temperatures but not at ambient conditions. This is accomplished by condensing and sub-cooling the liquid before it enters the metering device, with a low-temperature evaporator from one system serving as the condenser for the other.

1.2. Two Stage Cascade Refrigeration Systems:
Different kinds of compressor machines being employed in a two-stage cascade refrigeration system, they operated separately using dissimilar refrigerants and are connected such that the evaporator of the first cycle is utilized to chill the condenser of the second cycle. A practical solution is to use a shared capacitor and a booster circuit to produce two distinct evaporator temperature limits.
Using ultra-low-grade heat at 45°C – 60°C, the unique cascade system can easily refrigerate. The unique Vapour Absorption System (VAR) subsystem is in charge of the system's functioning. To improve its effectiveness, there are appropriate $T_m$ and $T_{g1}$. $T_{g2}$ has a greater influence on the appropriate $T_m$ while having little influence on the appropriate $T_{g1}$. [14]. For all three environmentally friendly refrigerants, the optimal generator temperature of its Hybrid cascade refrigeration system (HCRS) was observed to be the same [16]. In comparison to the traditional method, an ejector enhanced system had to have a faster pull-down time as well as a lesser freezer air temperature during continual process. At the appropriate freezing point of -40°C, the pull-down rate was determined by 34.4 %, and the compressor's usage of energy was reduced by 29.6 % [3].

The COP amplification of cascade systems was enhanced using a steady cooling rate of 100 kW inside the evaporator. When compared to the results obtained for pure refrigerants, COP goes from 18% to 32% post-optimization. The R744/RE170 blend produced the greatest results, with a COP of 2.34, a rise in exergy efficiency of up to 30%, and lower refrigerant flow rates ranging from 6% – 34%, compressor power ranging from 20% – 23%, and exergy destruction rate ranging from 31% - 36% [7]. When comparing to the EETCR system, the new ejector expansion transcritical cascade refrigeration (NEETCR) system exhibited a greater coefficient of performance and system second law efficiencies. Whenever the cooling capacity and operating parameters of the two systems had been the same, the COP and exergy efficiency of the NEETCR system improved by more than 9% when comparing to the EETCR system [9].

The non-dominated sort genetic algorithm-II (NSGA-II) methodology is used to optimize the cumulative exergy destruction (ED$_t$), total yearly cost (C$_t$), and multi-objective optimizing technique (C$_t$ and ED$_t$). ED$_t$ is 11% higher than the least result within the optimization technique aiming for a total yearly cost, indicating that the technique's thermal performance is inadequate. C$_t$ in the
optimization technique aiming at 100% exergy destruction is 14.8% higher than its least outcome, indicating that the system is costly. In the multi-objective optimization technique, $C_t$ and $ED_t$ were just 5.9% and 4.5% higher than their lowest outcomes, correspondingly. [10]. Introducing NH$_3$ rather than Propane as in the EEC-VCC system greatly improves the overall safety of the system. For a first inference, although using an ejector expander inside the NH$_3$/CO$_2$ or Propane/CO$_2$ BC-VCC system improves thermodynamic and economic parameters, it reduces the plant's risk dramatically [11]. A hybrid model with such a performance (COP) of 0.226 may provide a cooling load of 60.65 kW. This system's evaporation temperature also becomes determined to be -54.62°C. The overall exergy efficiency of the system is estimated to be 69% depending on the outcomes of the exergy assessment. In addition, 83.4 kW achieves the total exergy destruction rate, and also the rectifier has the maximum value of irreversibility (16.05 kW) [17].

2. Ultra-low temperature refrigerator storage

Blood and blood components, medicinal compounds, drugs, enzymes, and other biological products are stored in ultra-low temperature refrigerators or ULT refrigerators. They're utilized at hospitals, research institutions, blood banks, and other places in the healthcare business. Over the projected period during 2020-2030, the ultra-low temperatures refrigerator industry is poised to boost at a compound annual growth rate (CAGR) of 4.4 percent. Expanding R&D initiatives between leading companies, as well as government backing for scientific cases, had proved to be drivers for the ultra-low temperature refrigerator industry's growth. Among all of these reasons, the COVID-19 epidemic has a significant beneficial impact. As a result of the epidemic, the need for blood product components has skyrocketed all across the world, bolstering the ultra-low temperature refrigerator industry.

2.1 Ultra-low Temperature Refrigerators: Segmentation

| S. No | METHOD                        | TEMPERATURE RANGE | APPLICATION          | END USER                  | REGION        |
|-------|-------------------------------|-------------------|----------------------|---------------------------|---------------|
| 1     | Upright Ultra-low Temperature Refrigerators | -41°C to -86°C   | Blood & Blood Products | Biobanks                 | North America |
| 2     | Floor standing                | -87°C to -150°C   | Flammable Materials   | Hospitals                 | Latin America |
| 3     | Benchtop/Under counter        | -                 | Biological Samples    | Pharmaceutical and Biotechnology Companies | Europe |
| 4     | Chest Ultra-low Temperature Freezers | -                 | Drug Compounds        | Academic and Research Institutes | Asia Pacific |

An ultra-low temperature refrigerator has been segmented by method, temperature range, application, end-user, and key regions.

The secondary refrigerator storage container aids businesses in maintaining frozen quality standards and preparing for the unanticipated. With the worldwide frozen food industry expected to increase through 2024, cold storage firms simply can't afford their goods if they want to stay competitive and meet customer demand.

The frozen foods sector isn't the only one that's expanding globally. The worldwide vaccination business is expected to reach $100 billion in 2025, with some of these vaccinations requiring freezer...
storage. All around the world, there is a need for effective pharmaceutical items and good storage guarantees that these medications are viable and usable.

3. **Common applications of ultra-low temperature storage system**

Materials that require consistent freezing temperatures are stored in ultra-low temperature freezers. Unlike standard kitchen refrigerators, which should have been held at -18°C, an ultra-low temperature refrigerator allows for more accurate temperature regulation, ensuring that items are better protected from temperature changes. Blood banks, hospitals, research institutions, pharmaceutical production facilities, cold storage facilities, and food processing and packaging industries all employ ultra-low temperature freezers.

3.1 **Pharmaceuticals**

Several pharmaceutical items, such as vaccinations and antibiotics, should be kept in ultra-low temperature refrigerators. All varicella-containing vaccinations, for example, should be kept at a temperature of -50°C to -15°C and kept frozen until used. Some vaccinations, such as the MMR (measles, mumps, and rubella) vaccination, can be kept in refrigerators. Pharmaceuticals require serious storage to ensure that they remain safe and reliable. Inadequate storage might result in the waste of valuable materials as well as the high expense of revaccination. In Ventura County, for example, 23,000 individuals were given immunizations that were not adequately kept in 2017. As a consequence, over 1,000 patients were revaccinated. It would have cost $1.3 million to revaccinate all 23,000 individuals.

3.2 **Biological Samples**

The correct preservation of biological samples such as blood and plasma necessitate the use of ultra-low temperature freezers. Plasma, for example, must be kept at a temperature of -18°C or below until it is thawed. The blood and plasma, as well as their vital components, are preserved by freezing, ensuring a continual supply of life-saving transfusions.

3.3 **Food**

To keep products like ice cream, frozen goods, meats, and shellfish safe, cold storage freezers are required. Ultra-low temperature freezers can be used by food industry firms, from producers to merchants, to keep commodities including fish, meats, fruits, and vegetables fresh. Companies may freeze almost any product to preserve it, except for canned goods and eggs in shells.

3.4 **Benefits of Ultra-Low Temperature Storage**

- **Continued storage at ultra-low temperature levels**: Organizations don't have to worry about system failure when they use a dependable ultra-low temperature refrigerator vessel like the NMF-372. Our unit is equipped with two independent refrigerator systems that operate as backups in the event of one failing, guaranteeing that your cargo remains frozen and safe. Pharmaceutical medicines must be kept refrigerated at all times since even the tiniest temperature change can cause them to lose their potency.

- **Keep items at the proper temperature**: Temperature management is simplified with our high-quality ultra-low temperature storage container. Companies can keep items at exact temperatures with the easy-to-use interface and digital display.

- **Increased freezing capacity**: An ultra-low temperature refrigerator container gives you more room to freeze more merchandise, which is ideal for the busy season. Refrigerator units can also be placed strategically to improve worker productivity and decrease processes.

- **Using additional refrigerator storage capacity to extend the shelf life of items rather than trashing them**: Instead of throwing a surplus of items, you may use additional refrigerator storage space to extend the shelf life of items.
• **Customers receive high-quality products:** Food is kept at ultra-low temperatures to retain its quality of freshness. Customers love food that tastes as though it came straight from the ocean or the farm, and they'll recall that level of excellence the next time they purchase or buy frozen foods.

• **Long-lasting and safe storage:** Our freezers are made to last and keep items safe. Because we don't utilize wood in the construction of our refrigerator storage containers, they're resistant to decay and moisture damage.

4. **Several refrigeration methods in cascade**

The cascade refrigeration method consists of four systems:

1. Two-Stage Compression Refrigeration Method
2. Cascade Absorption Refrigeration Method
3. Compression–Absorption Cascade Method
4. Refrigeration Method with an auto-cascading effect.

Two-Stage Compression Refrigeration Methods are made up of two Single-Stage Compressive Cascading Refrigeration Systems that may reach a temperature around -80°C for evaporating. A low evaporating temperature can also be achieved using the Cascade Absorption Refrigeration Method using two Individual Cascade Absorption Refrigeration Systems. A heat exchanger cascades a Solitary Cascade Refrigeration System and a Single-Stage Absorption Refrigeration System in the Compression–Absorption Cascade Method. An evaporative condenser ensures a cascade among high and low boiling point elements in the refrigeration method with an auto-cascading effect; it has large potential applications and can easily achieve low evaporation temperatures under -40°C. The supplementary fluids and temperature limits for the different Cascade Refrigeration Systems are shown in Table 2. (CRS). We will introduce these four distinct CRSs in this section.

| S. No | Cycle Methods                                      | Working Fluids            | Temperature Range |
|-------|----------------------------------------------------|---------------------------|-------------------|
| 1     | Two-Stage Compression Refrigeration Method         | R744, R717, R134a, Zeotropes and Azeotropes Mixtures | -60°C to -100°C   |
| 2     | Cascade Absorption Refrigeration Method            | R717, LiBr-H₂O, NH₃-H₂O   | < -45°C          |
| 3     | Compression–Absorption Cascade Method              | R717, LiBr-H₂O, R744      | -35°C to -50°C   |
| 4     | Auto-cascading method                              | R23, R50, N₂, R170, R290 | < -55°C          |

4.1 **Two-Stage Compression Refrigeration Method:**

The Two-Stage Compression Refrigeration Method is made up of two independent subsystems; a High-Temperature Circuit (HTC) that uses NH₃ or any other Zeotropes and Azeotropes mixtures as a refrigerant, and a Low-Temperature Circuit (LTC) that uses CO₂ or any other Zeotropes and Azeotropes mixtures as a refrigerant. Each cycle has a compressor, the condenser, an expansion valve, and also an evaporator, and they are linked via a heat exchanger, that serves as both the condenser as well as the evaporator in the HTC and the LTC at the same time.
Figure 2. Two – Stage Compression Refrigeration System

When comparing to a Single-stage compression system, this approach offers the following advantages:

1. This system saves energy by allowing the use of refrigerants with appropriate temperature properties for both low and high-temperature cycles.
2. It enables ultra-low-temperature functioning that is stable.
3. The operating costs are low.
4. It's simple to fix.

4.1.1 Various Alterations to a Two-Stage Refrigeration Cycle:

Many efforts were made to reinvent CRS to improve performance. For example, to improve cascade efficiency, several high-energy-efficient approaches were proposed, including replacing the expansion valve with an internal heat exchanger or expander. Additionally, using a two-phase ejector instead of traditional expansion devices enhance CRS performance dramatically.

4.1.1.1 Ejector–expansion cascade refrigeration cycles:

An ejector is just a mechanical instrument that utilizes a higher pressure and velocity fluid to convert a least-pressure fluid to a highest-pressure fluid at such a diffuser output. The ejector had gained significant popularity due to its inexpensive cost, lack of moving parts, and capacity to handle two-phase fluid without destroying it. The need for an ejector will not only increase the cooling load while lowering compressor energy, but it can also retrieve expansion process loss through an isentropic expansion, improving the performance of a cascade system.
Cascade Absorption Refrigeration Method (CARM) is based on STARS and uses the evaporator from HTC to chill the condenser in LTC to achieve a lower evaporating temperature. The NH$_3$-H$_2$O system and a LiBr-H$_2$O system make up CARM. In LiBr-H$_2$O HTC, an evaporator is utilized to chill the condenser. In NH$_3$-H$_2$O HTC, its evaporator is utilized to chill the condenser.
4.2.1 The Various Cascade Systems Based on Design:

An absorption cooling system is a cost-effective method of recovering waste heat and reducing energy use. The cascade approach is a good strategy to enhance the absorption refrigeration system's performance. A Rankine cycle and also an absorption refrigeration circuit, as an example, have been suggested as a cascade. Excess waste heat HTC is utilized to generate electricity, whereas the LTC is utilized for refrigeration. Additionally, the refrigeration module retrieves the power subsystem's remaining heat. A simulation demonstrates that, as compared to the single power as well as refrigeration system, the system's energy usage is decreased by 17% at the same power output.

4.3 The Compression–Absorption Cascade Method:

Another type of CRS is the Compression Absorption Cascade Method, which may significantly improve performance over a traditional refrigeration system. Several compression absorption cascade methods are mostly powered by heat sources such as engine exhaust gases, industrial waste heat, solar energy, etc. Such systems may attain a low-temperature cooling capacity (between -40 and -50°C) without the use of power or energy.

![Figure 5. Compression - Absorption Cascade Method](image)

4.3.1 Various Alterations to a Compression-Absorption Methods:

Researchers have developed several attempts to improve cascade refrigeration systems to improve performance. The homogenization of a compression–absorption cascade refrigeration technology with an organic Rankine cycle, for example, efficiently saves energy for the ecosystem. In a compression–absorption double-stage (CADS) system, connect a second economizer as well as a condenser–generator to an absorption cycle may improve the system's Coefficient of Performance (COP).

1. Combined vapour compression–absorption cascade method and organic Rankine cycle.
2. A solar driven dual-evaporator vapour compression–absorption cascade method.
3. The compression–absorption cascade method powered by a cogeneration system.
4.4 Auto-Cascading Method.

![Auto-Cascading Method Diagram](image)

The concept entails using multiple mixed working fluid formulations under various pressure procedures as well as varied vaporizing and condensing temperatures. Auto Cascading Method has a large potential application with a low temperature of around -60°C for its design and operating dependability with high-performance level. For the use of -80°C freezing, an ejector improved two-stage auto-cascade refrigeration cycle (EARC) employing the compound mixtures R600a/R32/R1150 is suggested. In terms of the highest COP, the findings show that the ternary combination R600a/R32/R1150 does have the ideal mass fraction ratios of 0.45/0.2/0.35. In terms of COP, exergy efficiency, and volumetric refrigeration capacity, an EARC circuit outperforms the CARC cycle. In comparability to the CARC cycle, the EARC cycle showed a 4.9 percent–36.5 percent increase in COP and a 6.9 percent–34.3 percent increase in exergy efficiency [18].

4.4.1 Various alterations to auto cascading methods
1. An auto-cascade ejector refrigeration method
2. A low-temperature absorption–compression cascade system

5. Types of refrigeration systems
Numerous concepts are being devised to achieve the refrigeration effect, and as a result, different refrigeration systems are being devised. Every refrigeration system does have its own set of benefits and drawbacks, as well as a unique application. Vapor compression refrigeration methods and sorption refrigeration systems seem to be the most prevalent refrigeration systems that may be utilized for several purposes. Furthermore, solar energy may be utilized in a variety of ways like vapour compression refrigeration cycle, photovoltaic cell operated refrigeration cycle, solar mechanical refrigeration, sorption refrigeration technologies, absorption systems and adsorption systems.
6. Discussion

The variation in the Coefficient of Performance among R134a and R32 is 0.71 percent, as well as the exergetic efficiency is 1.31 percent, which isn't much of a difference considering the distinction among R32 and R1234yf is 1.2 percent and 2.23 percent, correspondingly. While R1234yf has an environmental advantage over both refrigerants, it cannot be employed in ultra-low operating temperatures. As a result, for ultra-low operating temperatures, R32 is the better option than R134a from an environmental standpoint [16]. Moreover, lots of HFO and HFC refrigerants with zero ODP and GWP need to be analyzed.

Three factors of energy, exergy, & economy are used to evaluate the performance of a system. To optimize the Cascade Absorption Refrigeration (CAR) system, overall exergy destruction and entire year cost are often used as goals. The impacts of different operational settings upon this system's thermodynamic characteristics and costs are studied. Increasing the temperature of LiBr-H\textsubscript{2}O evaporation and the NH\textsubscript{3}-H\textsubscript{2}O condensation and absorber can improve economic performance (by reducing total heat transfer and total yearly cost), but this will degrade thermodynamic effectiveness. [4]. Decreasing the LiBr-H\textsubscript{2}O condenser temperature would give better performance than increasing the LiBr-H\textsubscript{2}O evaporator temperature.

The experimentally measured COP of a cascade system had been compared to a COP with multiple NH\textsubscript{3} cascade systems: a system with twin compression stages and a flash tank economizer, and a system with twin compression stages and inter cooling in a flash tank (intercooler), both using NH\textsubscript{3} as a refrigerant. It's been shown that at evaporation temperature below -35°C, systems using NH\textsubscript{3} as a refrigerant provided evaporation pressures lesser than atmospheric pressure, but the evaporation pressure acquire from the cascade system have always been greater. According to the findings of the total COPs of the evaluated refrigeration systems at -40°C evaporation temperature or below, the cascade system, with a COP value of close to 19.5 percent higher, appears to be the most beneficial alternative. [5]. Instead of a flash tank economizer, an ejector system may give more COP than this system.

For both HTC and LTC, the usage of blended refrigerants resulted in a greater COP than systems running on a single refrigerant. The ability to influence mixed refrigerant compositions has given the system a new level of flexibility, allowing it to change the refrigerant's characteristics to improve system performance for the use presented or to widen it to various applications by modifying the concentration. The best pair for a CRS running with blended refrigerants to maximize global COP is R744/RE170, which uses 20 wt% R744 in the HTC and 10 wt% R744 in the LTC, taking into account not only the highest COP as well as some important operational requirements such as a lower discharge temperature and low condensation pressure. [7]. Even though many Zeotropic and Azeotropic refrigerants are better options for the cascade refrigeration system to enhance its performance.

Over the last several years, several ways to improving the performance of the cascade refrigeration system have been developed, with the most outstanding innovations being the use of an ejector expander rather than a normal expansion valve. However, while such analysis improves energy and exergy effectiveness as well as the system's unit price, the plant's safety is significantly reduced owing to the usage of combustible or hazardous refrigerants inside the cycle. Although more research is being done on the function of the ejector expansion in terms of energy, exergy, exergoeconomics, and the environment, no quantitative risk assessment (QRA) of ejector expansion cascade refrigeration systems has been done [11]. The ejector expands cascade refrigeration system with subcooling and superheating will enhance the performance of a cascade refrigeration system.
7. Conclusion

Various types of Cascade Refrigeration Systems (CRS) were developed; nevertheless, the system challenges are more than with a traditional Single-Stage Refrigeration System. When compared to the two-stage vapor Compression Cascade Methods, the Compression Absorption Cascade Method is now a high-performance system. Additionally, due to its lower system difficulties, an ejector–expansion CRS is a wonderful option.

Even if the cascade refrigeration system may greatly expand the freezing temperature province, it also increases the system's manufacturing cost and difficulties. Additionally, as the system's complexity grows, so does the difficulty of its repair and control.

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