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Novel Cascade Refrigeration Cycle for Cold Supply Chain of COVID-19 Vaccines at Ultra-Low Temperature −80°C Using Ethane (R170) Based Hydrocarbon Pair

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Abstract

Several media report highlight on that the pharmaceutical companies require ultra-low temperatures −80°C to transport and store its COVID-19 vaccines. This research presents the thermodynamic analysis on cascade refrigeration system (CRS) with several refrigerant pairs which are R32/R170, R123/R170, R134a/R170, R404A/R170, R407c/R170, R410/R170, and the hydrocarbon (HC) refrigerant pair Propane/Ethane, namely R290/R170. Besides, the results of R22/R170 pair, which is not recommended to be used due to phase out of R22 as per Montréal Protocol, are included as base case to compare the novel hydrocarbon pairs in CRS and the old trend of refrigerant pairs. Thermodynamic properties of all these pairs were investigated and compared under different intermediate temperature used in CRS heat exchanger, which thermally connected both the Low and High temperature cycles (LTC) and (HTC). By applying the first law of thermodynamics, the coefficients of performance (COPs) and the specific power consumptions (SPC) in kW/TR are presented and compared. In addition, by applying the second law of thermodynamics the exergetic efficiencies were estimated. The results reveal the promising opportunity of using the HC pair (R290/R170). The minimum SPC in kW/TR is recorded for the pair R123/R170. One the other hand, the highest exegetic efficiency values are observed to be 40%, 38%, and 35% for the pairs R123/R170, R290/R170, and R134/R170, respectively. This research concludes that the HC pair (R290/R170) is highly recommended for CRS applications either to transport the COVID-19 or store it in cold storage rooms in hospitals and clinics. All precautionary measures should be carefully applied in design and operation of HC pair (R290/R170) due to its flammability hazard.
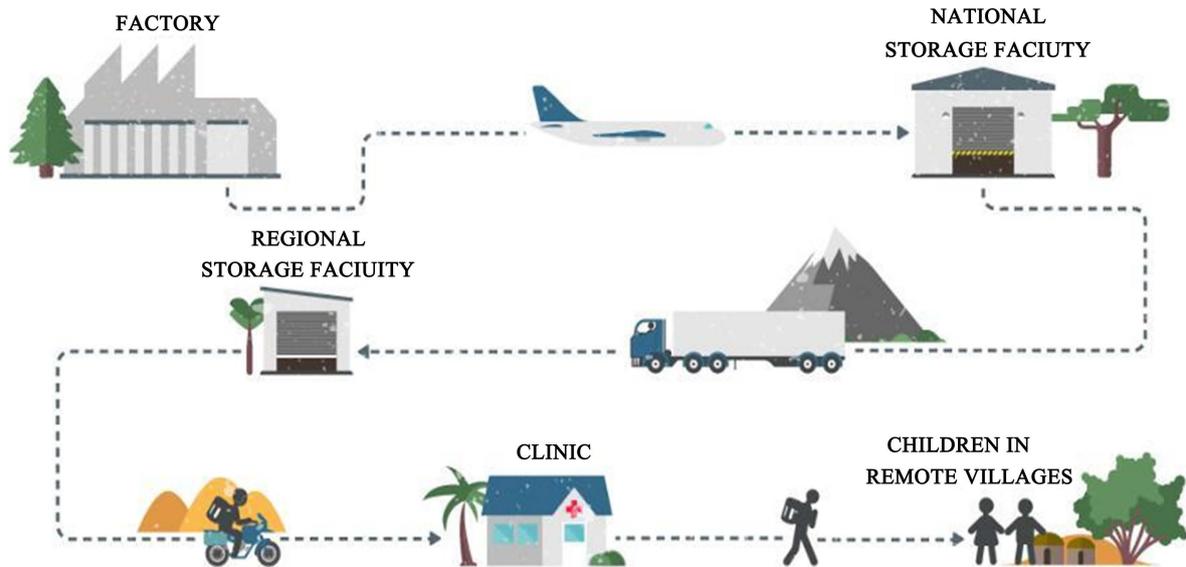
1. Introduction

As the world gears up to produce and distribute the COVID-19 vaccines, the vaccines are gradually moving closer to becoming available. Scientists around the world developed vaccines for COVID-19 in record time, which is less than a year, the race is on to inoculate the greatest number of people in the shortest time as reported by Wood [1]. The transportation and storage processes for some vaccines require license for distribution which may complicate the existing supply chains and make them more challenging. This is particularly true of cutting-edge mRNA vaccines, which must be kept at constant super-low temperatures to avoid spoiling: as low as −170˚F ahrenheit. Recently, several researches have been conducted on vaccine production, transportation, storage techniques, and influences on peoples in different ages, countries, gender, and health conditions. Even though COVID-19 vaccines are being developed more quickly than usual, vaccine safety is still a top priority in all phases of vaccine development, approval, and post-approval monitoring. On the other hand, more traditional viral vector vaccines can be produced, transported and stored around 40˚F, making use of existing cold chain logistics infrastructure. **Figure 1(a)** displays the COVID-19 vaccine supply chain challenges in its long journey starting from the factory to national storage facility, to regional storage facility, to clinics, and at the end to reach all children and adult also in remote villages, as presented by Biyani [2]. **Figure 1(b)** depicts the infographic in which comparison between cold supply chain 1 dedicated for mRNA vaccine, and cold supply chain 2 dedicated to viral vector vaccine presented by Wood [1]. **Figure 1(b)** classifies the two different cold supply chain journeys for two different vaccines, highlighting the issues that distributors must overcome to safely transport their medical marvels around the world. **Figure 1(c)** demonstrates the proposed vaccination plan in India, presented by Kaul [3], based on three phases which are: phase 1 for vaccine transportation, phase 2 for identifying, issuing shots, and phase 3 for follow up after vaccination.

The rest of the paper proceeds as follows. Section 2 presents the literature review which is classified into four main parts for cascade cycle optimization, using different refrigerant types in cascade refrigeration cycle, innovation for cascade refrigeration system components, and finally the vaccine transportation and production requirements. Then, the research objectives are clearly presented to cover the research gap and to answer the research highlighted question. Section 3 presents the materials and methodologies used in the current research.

The long road to vaccination

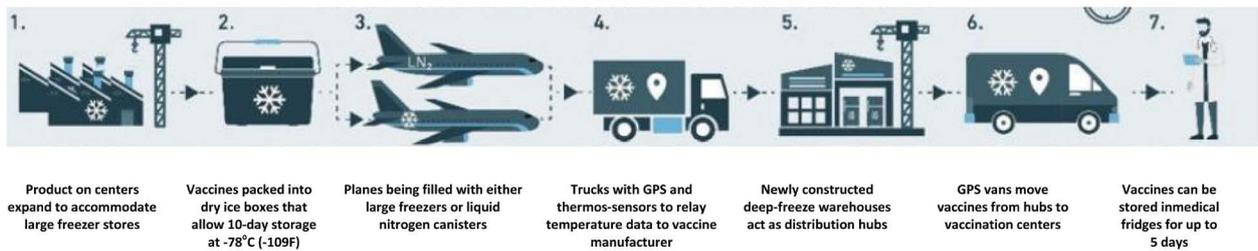Vaccines must be kept between 2°C - 8°C all the way from the factory to some of the most remote places on earth.

FACTORY

NATIONAL
STORAGE FACIUTY

REGIONAL
STORAGE FACIUITY

CLINIC

CHILDREN IN
REMOTE VILLAGES

Source: MSF

(a)

Cold Supply Chain 1: mRNA Vaccine
Shipments must maintain temperatures between −78°C (-109F) and −20°C (−4F) from manufacturer to end user.
This requires the construction of new warehouses and upgrading of air and road transport.

1.	2.	3.	4.	5.	6.	7.
Product on centers expand to accommodate large freezer stores	Vaccines packed into dry ice boxes that allow 10-day storage at -78°C (-109F)	Planes being filled with either large freezers or liquid nitrogen canisters	Trucks with GPS and thermos-sensors to relay temperature data to vaccine manufacturer	Newly constructed deep-freeze warehouses act as distribution hubs	GPS vans move vaccines from hubs to vaccination centers	Vaccines can be stored inmedical fridges for up to 5 days

Cold Supply Chain 2: Viral Vector Vaccine
Shipments must maintain temperatures between −78°C (-109F) and −20°C (−4F) from manufacturer to end user.
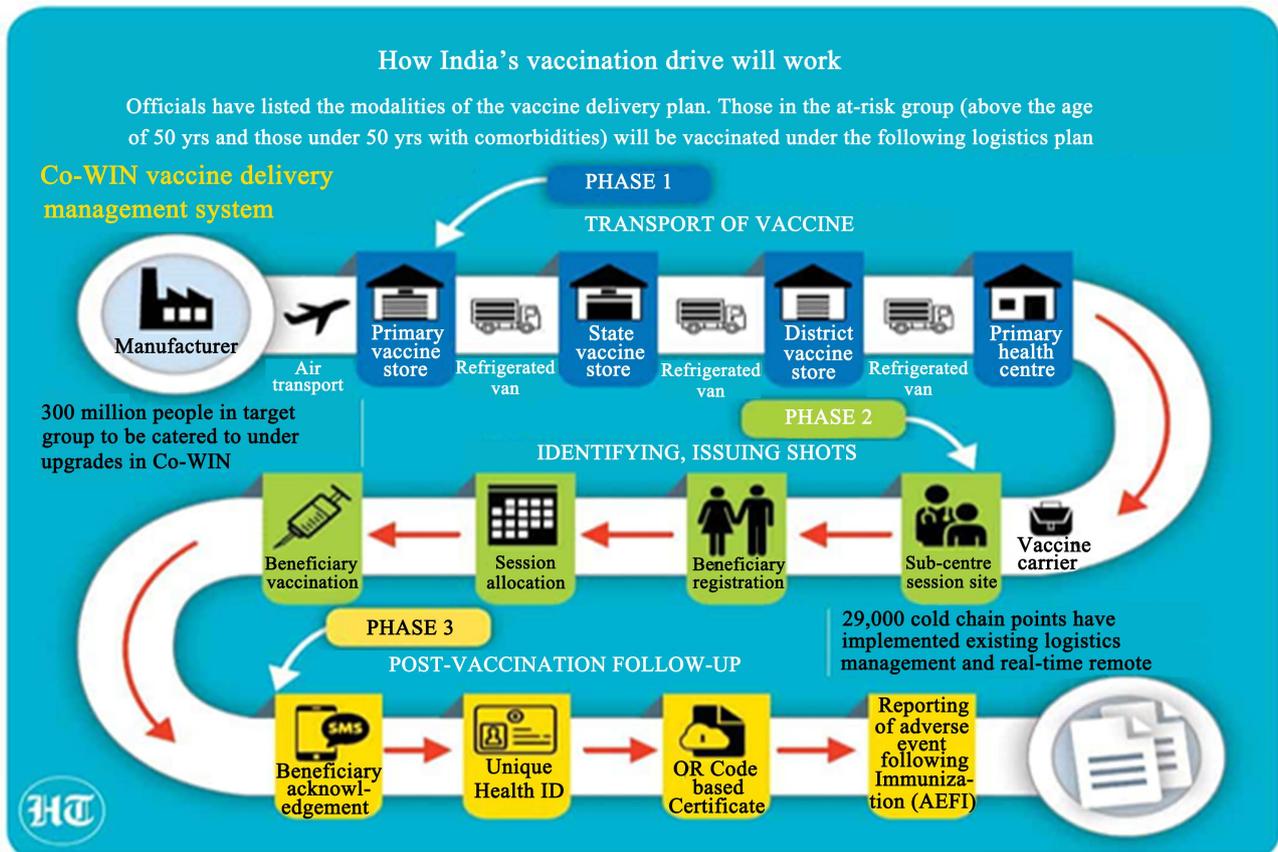This requires the construction of new warehouses and upgrading of air and road transport.

1.	2.	3.	4.	5.	6.
Existing facilities can easily scale up to meet demand	Existing cold chain refrigerated trucks keep vaccines between 2°C (35F) and 8°C (46F)	Vaccine can be shipped normally on plane without refrigeration	Existing warehousing and logistics hubs can be used for distribution	Vaccines can be moved without the need for temperature monitoring	Vaccines can be stored for long periods

(b)

Figure 1. The COVID-19 vaccine supply chains, and vaccination plan and long road from factories to Clinics. (a) COVID-19 vaccine supply chain long road challenges presented by Biyani [2], (b) Classification of vaccine supply chains presented by Wood [1], and (c) transportation to jabs center outlines COVID-19 vaccination plan in India presented by Kaul [3].

The materials are classified into three subsections which are Classification of COVID-19 vaccines, classification of cold storage and refrigeration machines, and theory of operation for cascade refrigeration cycle. Then the current research methodology is described. The results and discussion are presented in Section 4. At the end of this article the recommendation and suggestions for Future work are explored and presented in Section 5.

2. Literature Review

This section described the current literature review which is divided into two main parts; the first part, listed in Subsections 2.1, 2.2, and 2.3, is for Engineering and technologies for cascade refrigeration systems (CRS) in providing ultra-low temperature for many applications, and the part second, listed in Subsection 2.4, is for the medical and pharmaceutical demand for ultra-low temperature to keep, store and transport the COVID-19 vaccine. The first part is classified into three research groups based on their research interests. The first group, listed in Subsection 2.1, focuses on the optimization of cascade refrigeration cycles. The second group, listed in Subsection 2.2, focuses their interest on the

influence of using different refrigerant types on the energy and/or exergy performance of cascade refrigeration cycle. However, the third group, listed in Subsection 2.3, focuses on innovation of cascade refrigeration systems using advanced system components and cycle arrangements and/or configuration. At the end of this section, the research objective, listed in Subsection 2.5, is clearly highlighted to cover the currently observed research gap.

2.1. Cascade Refrigeration Cycle Optimization

Wang *et al.* [4] experimentally investigated the pull-down performance of a −80°C ultra-low temperature freezer. They concluded that the volumetric efficiency of high temperature cycle (HTC) compressor deteriorated more obviously during the pull-down process, and had higher potential for performance improvement compared with that of LTC. Ustaoglu *et al.* [5] optimized the performance of a vapor compression cascade refrigeration cycle by considering the statistical analysis methods, Taguchi and ANOVA approaches. They concluded that the COP and exergy efficiency within the range of the operating parameters in the evaluation were found to be 3.274% and 37.63%. Rui *et al.* [6] proposed a novel ternary mixture, R600a/R23/R14, for ARC systems for 190 K (−83°C) applications. Their results demonstrated the feasibility of the proposed R600a/R23/R14 ternary mixture as an environmental benign alternative for Auto-Refrigeration cascade systems. Roy and Mandal [7] numerically investigated energetic, exegetic, economic and environmental performances of a 50-kW cooling capacity cascade refrigeration system using four different refrigerant pairs, namely R41/R404A, R170/R404A, R41/R161 and R170/R161. They conclude that the COP and exergetic efficiency of the system to be maximum with R41/R161 refrigerant pair followed by R170/R161 for the same operating conditions.

2.2. Influence of Refrigerant Types on Cascade Refrigeration Cycles

Roy and Mandal [8] conducted a numerical study of cascade refrigeration system using two different refrigerant pairs, namely, R41/R404A and R170/R161. They concluded that R170/R161 is in higher optimal COP as well as exergetic efficiency for system compared to R41/R404A system. The refrigeration performance parameters of two binary azeotropic mixtures of R170/R23 and R170/R116 and a ternary azeotropic mixture of R170/R23/R116 were measured systematically in the low-stage loop of a two-stage cascade system by Gong *et al.* [9]. They concluded that these mixtures show good potential as low-temperature stage refrigerants for applications in the −80°C temperature range. Zou *et al.* [10] experimentally investigated the heat transfer coefficients for saturated flow boiling in a horizontal tube of the binary mixtures of R170/R290. They conclude that the comparison of the experimental heat transfer coefficient with the predicted value shows that the total mean deviation is 15.97% for R170/R290 mixtures. Zhuang *et al.* [11] compared experimental data with various well-known correlations of condensation heat transfer coefficient and pressure drop of R170 in a horizontal

tube with inner diameter of 4 mm. Chen *et al.* [12] conducted a theoretical study on a modified vapor compression refrigeration cycle (MVRC) with zeotropic mixture R170/R290 for freezers. They concluded that the proposed cycle has potential advantages for application in the freezers. Park and Jung [13] presented the thermodynamic performance of R170/R290 mixture on a heat pump bench test in an attempt to substitute R22. They conclude that the coefficient of performance (COP) and capacity of R290 are up to 15.4% higher and 7.5% lower, respectively than those of R22 for two conditions. Sun *et al.* [14] presented a comparative analysis of thermodynamic performance of cascade refrigeration systems (CRSs) for refrigerant couples R41/R404A and R23/R404A to discover whether R41 is a suitable substitute for R23. They concluded that the theoretical analysis indicates that R41/R404A is a more potential refrigerant couple than R23/ R404A in CRS. Sun *et al.* [15] investigated the suitability of using R23, R41 and R170 in the low-temperature cycle (LTC) and R32, R1234yf, R1234ze, R161, R1270, R290 and R717 in the HTC refrigerant in CRS. They recommended R161 for use in HTC, and R41 and R170 for use in LTC. Nawaz *et al.* [16] evaluated the performance of R290 (propane) and R600a (isobutane) as substitutes for R134a (a HFC) for heat pump water heating (HPWH). They concluded that a significant reduction in system charge and lower condenser discharge temperatures as additional benefits. Liu and Yu [17] proposed the using of an ejector subcooling refrigeration cycle (ESRC) with zeotropic mixture R290/R170 for low temperature freezer applications. They conclude that the performance characteristics of the proposed cycle demonstrate its potential applications in low-temperature freezers. Aktemur *et al.* [18] proposed using R41 in low-temperature circuit (LTC), and using R1243zf, R423A, R601, R601A, R1233zd (E) and RE170 for a high-temperature circuit (HTC). They concluded that there is a maximum COP improvement of 13.05% compared to studies in the literature. Turgut and Turgut [19] presented a comparative investigation on performance analysis of cascade refrigeration systems using R744/R717, R744/R134a, and R744/R1234yf refrigerant pairs. Das and Samanta [20] conducted a comparative analysis on energy and exergy of cascade refrigeration system using different pairs of refrigerants. They concluded that R744/R717 attained the highest COP value equivalent to 7.848, and the highest ECOP value of 0.9838 was also attained by R744-R717. Xie *et al.* [21] proposed using the pairing consists Hydrocarbons, such as R170 and R290 as natural working fluids instead of R22/R23 in cascade refrigeration cycles. They concluded that R290/R170 can be used as the substituting refrigerants to R22/R23 in the cascade refrigeration cycle. Wang *et al.* [22] investigated the performance of a single-stage Linde-Hampson refrigerator (LHR) operating with six different binary refrigerants (R23/R134a, R23/ R227ea, R23/R236ea, R170/R290, R170/R600a and R170/R600) with ozone depletion potentials (ODPs) of zero was conducted using a new approach at the temperature level of −60˚C. They introduced two useful new parameters, the entropy production per unit heat recuperated and the ratio of heat recuperating capacity to the power consumption of the compression. Fatouh and El Kafafy

[23] conducted an investigation on Liquefied petroleum gas (LPG) of 60% propane and 40% commercial butane to substitute for R134a in a single evaporator domestic refrigerator with a total volume of 10 ft³ (0.283 m³). Their results reveal that lower on-time ratio and energy consumption of LPG refrigerator are observed by nearly 14.3% and 10.8%, respectively, compared to those of R134a refrigerator were achieved. They conclude and proposed using LPG as an appropriate long-term candidate replacing R134a in the domestic refrigerators, except capillary tube length and initial charge.

2.3. Innovation for Cascade Refrigeration Cycles

Pan *et al.* [24] provided a literature review of the cascade refrigeration system (CRS) to achieve an evaporating temperature as low as −170˚C. Jain *et al.* [25] developed a thermodynamic model for cascaded vapor compression–absorption system (CVCAS) which consists of a vapor compression refrigeration system (VCRS) coupled with single effect vapor absorption refrigeration system (VARS). They use the first and second laws of thermodynamics to perform their comparative study for a design capacity of 66.67 kW. The results show that the for CVCAS the electric power consumption is reduced by 61% meanwhile the COP of vapor compression cycle is improved by 155%. Cheng *et al.* [26] conducted a novel double internal auto-cascade two-stage compression system suitable for refrigerant mixtures, which can effectively modulate the concentration of the refrigerant going to the evaporator and the injection port, drive the refrigerant rich in high-pressure composition to enter the evaporator, thereby improving the system performance. Dixit *et al.* [27] investigated the proposal of integration of a two-stage absorption refrigeration system with a compression refrigeration system for utilizing low-temperature heat and reducing electric energy consumption. They compared this proposed system with vapor compression system from the viewpoint of energy, exergy, environment and economics. The proposed system reduces the electricity consumption by 89.3%.

2.4. Vaccine Supply Chain Recent Requirements

Bulula *et al.* [28] proposed to use Medical Store Department (MSD) to the Expanded Program on Immunization (EPI) to reduce costs of the vaccine supply chain responsibilities in Tanzania. Zhao *et al.* [29] conducted their study on a mixed solution of tetradecane (TD) and lauryl alcohol (LA) was selected as the base liquid. They developed a new type of cold storage equipment for vaccine, which can monitor the temperature of the vaccine in real time on the user's mobile phone. They stated that coupling the developed low temperature phase change material with the cold storage equipment can ensure that the vaccine is always in the required low temperature environment. Recently, Holm and Poland [30] stated that it is important for providers to be familiar with the practicalities of vaccine packaging, storage, preparation, and administration. Several of these vaccines require ultra-cold or have cold-storage requirements that are different than what vaccine administrators are prepared for. More recently, Mou-

neer [31] conducted many case studies on health and safety applications to high-light the importance of sustainable development under COVID-19 in Egypt. These cross sectional studies included the COVID-19 transportation and vaccination plan in many countries.

2.5. Research Objective

The research objective is to compare different pairs of refrigerants included hydrocarbon refrigerant pair Propane/Ethane namely (R290/R170) to be used in cascade refrigeration systems (CRS) to cool down the evaporating temperature to store COVID-19 vaccines which may need keeping temperature either during transportation or during storage processes at low temperature reaches to −80°C. The aims of this objective is to evaluate the thermodynamic analysis on both the first law for COP values and the second law for exegetic efficiencies for the proposed alternatives consist of lower side and higher side refrigerant vapor compression cycles, which work together to achieve the cooling down the cold stores for COVID-19 vaccines along its journey through cold supply chain either in cold storage in cold in hospitals and clinics or in transportation via refrigerated tucks, ships, and aviation.

3. Materials and Methods

This section demonstrates the materials and methods of the current research such as; the classification of COVID-19 vaccines, types of cold stores for vaccines transportation and storage, cascade refrigeration systems and system components, and refrigerant classification tree. This research methodology is presented in this section.

3.1. COVID-19 Vaccines Classification

Holm and Poland [30] reported that each vaccine has different packaging and requirements for storage, preparation, and administration, as reported by. Recently, Shervani *et al.* [32] presented useful data and very important results in containing, treating and eliminating pandemic COVID-19. They Classified the COVID-19 vaccines according to its production companies, dosing, and storage requirements. More recently, Williamson [33] reported in one article on BBC that UK government have classified the COVID-19 vaccines into seven types of vaccines based on their origin countries in the as follows: 1) Oxford University AstraZenca of UK, 2) Moderna (mRNA−1273), 3) the Pfizer-BioNTech (BNT162b2), 4) Gam-COVID-Vac Sputnik V, the Russian vaccine, 5) Corona-Vac (Sinovac), the Chinese vaccine, 6) Novavax, the American vaccine, and 7) Johnson & Johnson (JNJ-78436735), as reported in BBC by Williamson [33], as can be seen in both Figure 2(a) and Figure 2(b). Figure 2(a) depicts the COVID-19 classification in tabulated form as shown in Figure 2(a). Meanwhile, Figure 2(b) compares between the final prices for most of these vaccines, using the bar chart for the cost per jab of COVID-19 vaccine candidates, presented by
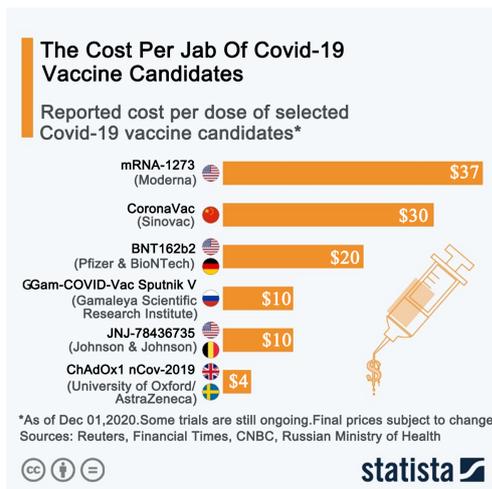
How some of the Covid-19 vaccines compare

Company	Type	Doses		Storage
Oxford Uni-AstraZeneca	Viral vector (genetically modified virus)	x2		2 to 8°C (6 months)
Moderna	RNA (part of virus genetic code)	x2		-25 to -15°C (7 months)
Pfizer-BioNTech	RNA	x2		-80 to -60°C (6 months)
Gamaleya (Sputnik V)	Viral vector	x2		-18.5°C (liquid form) 2 to 8°C (dry form)
Sinovac (CoronaVac)	Inactivated virus (weakened virus)	x2		2 to 8°C
Novavax	Protein-based	x2		2 to 8°C
Janssen	Viral vector	x1		2 to 8°C (3 months)

Source: UK government, Reuters

BBC

(a)

Leveraging the HIV Vaccine Enterprise for COVID-19 Vaccine Research

The Cost Per Jab Of Covid-19 Vaccine Candidates

Reported cost per dose of selected Covid-19 vaccine candidates*

- mRNA-1273 (Moderna) — $37
- CoronaVac (Sinovac) — $30
- BNT162b2 (Pfizer & BioNTech) — $20
- GGam-COVID-Vac Sputnik V (Gamaleya Scientific Research Institute) — $10
- JNJ-78436735 (Johnson & Johnson) — $10
- ChAdOx1 nCov-2019 (University of Oxford/AstraZeneca) — $4

*As of Dec 01,2020. Some trials are still ongoing. Final prices subject to change.
Sources: Reuters, Financial Times, CNBC, Russian Ministry of Health

statista

(b)

HIV vaccine research

- **Understanding retroviruses** — Tools that can analyze RNA viruses at the molecular level.
- **Vaccine administration: How vaccines get into the body** — Innovative injection approaches to improve immune responses.
- **Immune system research** — Decades of research into how RNA viruses and the immune system interact.
- **Vaccine platforms: How vaccines prompt the immune system** — Innovative methods for antigen presentation to improve immune responses and vaccine durability.
- **Community engagement** — Good Participatory Practices (GPP) pioneered in HIV research are informing COVID-19 research.
- **Research collaboration** — Building research collaboratives to speed R&D, share data and harmonize processes.
- **Clinical research capacity** — Leveraging existing HIV vaccine clinical trial site experience and capacity.
- **Funding collaborations** — Mobilizing HIV vaccine funders and funding mechanisms for accelerated COVID-19 vaccine development.

AVAC
25 Years and Counting

May, 18 2020
avac.org

(c)

Figure 2. Comparison for the specifications of the COVID-19 vaccines. (a) Type, Dose and storage requirements for the COVID-19 vaccine as classifed and reported by Williamson [33] reported in one article on BBC, (b) the cost per jab of COVID-19 vaccine candidates as reported in Dec 01 2020 by Reuters, Financial Times, CNBC, Russian Ministry of Health reported by McCarthy [34], (c) HIV vaccine enterprise for COVID-19 vaccine research as reported by AVAC [35] early in May, 18 2020.

McCarthy [34]. **Figure 2(c)** shows the HIV vaccine enterprise for COVID-19 vaccine research as reported by AVAC [35]. **Figure 3** shows the classification of the COVID-19 vaccines. **Figure 3(a)** displays the transportation container used to keep the COVID-19 vaccine in −80˚C, meanwhile **Figure 3(b)** shows the standard COVID-19 vaccine bottle. The first vaccine type, produced by the company Moderna named (mRNA−1273), which also acts on the mechanism of mRNA. It has dosing schedule consists of two doses, 28 days apart. This type requires Frozen between −13˚F to 5˚F (−25˚C to −15˚C). It can be stored refrigerated from 36˚F to 46˚F (2˚C to 8˚C) for up to 30 days prior to first use. Sinopharm's vaccine can be stored at 2 to 8˚C (36˚F to 46˚F), or a normal refrigeration temperature. The second vaccine is produced by Sino pharm company (China) named CoronaVac or SinoVac, as shown in **Figure 3(e)**. The third vaccine type produced by two joint venture companies Pfizer/BioNTech named (BNT162b2), as can be seen in **Figure 3(c)**, acts on the mechanism of mRNA. It has dosing schedule consists of Two doses, 21 days apart. This type requires Ultra-cold freezer works between −112˚F to -76˚F (−80˚C to −60˚C) for up to 6 months. The fourth vaccine is Russian vaccine and it has named Sputnik V. The fifth vaccine is produced by Johnson & Johnson/Janssen (JNJ) companies and it has named JNJ-78436735, as shown in **Figure 3(d)**. It has one dosing schedule and two-dose regimen is under evaluation. It is stable for 2 years at −4˚F (−20˚C) but can be stored for at least 3 months at typical refrigeration temperatures of 36˚F to 46˚F (2˚C to 8˚C). The sixth vaccine is the American vaccine and it is produced by Novavax company.

(a)   (b)

(c)   (d)   (e)

Figure 3. COVID-19 vaccines classification (a) Transportation Container to keep COVID-19 vaccine in −80˚C, (b) standard packing bottle for vaccine, (c) Pfizer vaccine (BNT162b2), (d) Johnson & Johnson (JNJ) vaccine, and (e) Sinovac vaccine (CoronaVac).

3.2. Cold Stores for Vaccines Transportation and Storage

Figure 4 presents the cold stores and freezers for transportation and storage for the COVID-19 vaccines. The vaccine refrigerators and refrigeration machines can be classified into three types according to energy sources as follows: 1) vapor compression units which are electric power driven machines as can be seen in Figure 4(a) and Figure 4(b), 2) photovoltaic units which use solar energy driven machines as can be seen in Figure 4(c), and 3) absorption units which named bottled gas or kerosene driven machines as can be seen in Figure 4(d). Ice-lined refrigerators are the preferred option where there is reliable mains electricity for at least eight hours per day. Even with periodic breaks in electricity, the inner lining of the unit can preserve the +2°C to +8°C holdover time. A few models are available that can operate effectively on as little as four hours of

(a) (b)

(c) (d)

(e) (f)

Figure 4. Cold stores and freezers for transportation and storage for the COVID-19 vaccines. (a) −80°C movable freezers for vaccine transportation, (b) −80°C vaccine freezer with double doors, (c) using solar energy for vaccine freezers, (d) freezers with top sliding doorway for vaccine, (e) cold store for vaccine storage, and (f) Mobile cold room (Trailer Container) for vaccine transportation.

electricity per day. Ice-lined refrigerators can expose vaccines to freezing temperatures if vaccines are not loaded properly. Solar energy refrigerators (photovoltaic units) are more expensive to buy and install than electric refrigerators, but they have no running costs, apart from cleaning and preventative maintenance. There are two types for solar refrigerators which are: 1) solar-battery units connected to a battery bank, which is charged by the solar panels, and 2) solar direct-drive units that are powered directly by the solar panels. Absorption units Bottled gas (or kerosene) refrigerators may be necessary in places where there is insufficient sunshine for a solar-powered unit. Gas-powered units are better than kerosene models because they need less maintenance and have better temperature control. Bottled gas and kerosene refrigerators can expose vaccines to freezing temperatures. Keeping vaccines in the +2˚C to +8˚C range is particularly difficult with kerosene refrigerator. Another classification for refrigerators and their types is presented according to mobility and transportation as follows: 1) Cooling stores (rooms) as can be seen in **Figure 4(e)**, and 2) Portable (Mobile) fridge as can be seen in **Figure 4(f)**. Outdoor events that affect vaccine can be a major concern without adequate cold storage containers with necessary cooling capacity. This is the very reason pharma companies recommend to use mobile fridge and cold storage solutions. Several refrigerated compartments and buildings were designed for storage vaccine in an environment below the outdoor temperature. Many vaccines must be stored at low temperatures, some below −15˚C (between −25˚C and −15˚C), and others between 2˚C and 8˚C. If vaccines are not stored correctly, they can lose their effectiveness.

3.3. Cascade Refrigeration Cycles

A cascade refrigeration cycle can be considered as a multi-stage compression thermodynamic refrigeration cycle. In the cascade refrigeration system, more than one vapor compression cycles (two or more) with more than one refrigerant are circulated as primary refrigerants. The evaporating and the condensing temperatures of both cycle are sequentially lower with some overlap to achieve the desired total temperature drop, with carefully selected refrigerants to efficiently work in the desired temperature range they have been designed to provide it together. The low temperature cycle absorb heat from the cold store to be cooled down using the low temperature cycle evaporator, then it transfers this removed heat to a heat exchanger, namely cascade condenser, is cooled by the evaporation of the refrigerant of the high temperature cycle. Therefore, the high temperature cycle transfers this amount of heat to the condenser of the high temperature cycle, to carry the rejected heat outside of the cascade refrigeration system, either using air cooled condenser associated with fans, or water cooled condenser associated with cooling water pumps and cooling towers. In the current thermodynamics analysis, a two-stage cascade system uses two pairs of compressor plants, working individually with different refrigerants, connected among themselves so that evaporator one system is used to serve as the capacitor to a lower temperature of the system (*i.e.* the evaporator with the first unit cools

the condenser of the second unit). In practice, an alternative approach utilizes a common capacitor with a booster circuit to provide two separate temperature of the evaporator. Clearly, diagram in two stages of the cascade refrigerating system, as shown that the compressor is reduced and the amount of cooling load (capacity) in the evaporator increases as a result of the cascade. **Figure 5** depicts the Cascade Refrigeration System (CRS), which is proposed in the current study as innovative refrigeration system for COVID-19 vaccines transportation and storage. **Figure 5(a)** and **Figure 5(b)** demonstrate the presentation of cascade refrigeration cycle (CRS) with its both individual cycles consists of low temperature cycle (LTC) and high temperature cycle (HTC) on T-s diagram and p-h diagram, respectively, as presented by Aktemur *et al.* [18], for both cycles LTC and HTC. **Figure 5(c)** shows line diagram for cascade refrigeration cycle with LTC and HTC, as presented by Alhamid *et al.* [36]. They conducted a study to investigate the characteristics and COP of cascade refrigeration system using hydrocarbon refrigerant (Propane, Ethane) and CO_2 at LTC. Their study constructed a prototype cascade refrigeration machine using the environmentally friendly hydrocarbon refrigerants (Propane, Ethane) and CO_2. Their results are that the characteristics of the pressure and temperature of each component and the COP value at low temperature circuit of load variations using an electric heater at 90 W, 120 W and 150 W result in a COP value of 0.35, 0.48 and 0.60, respectively.
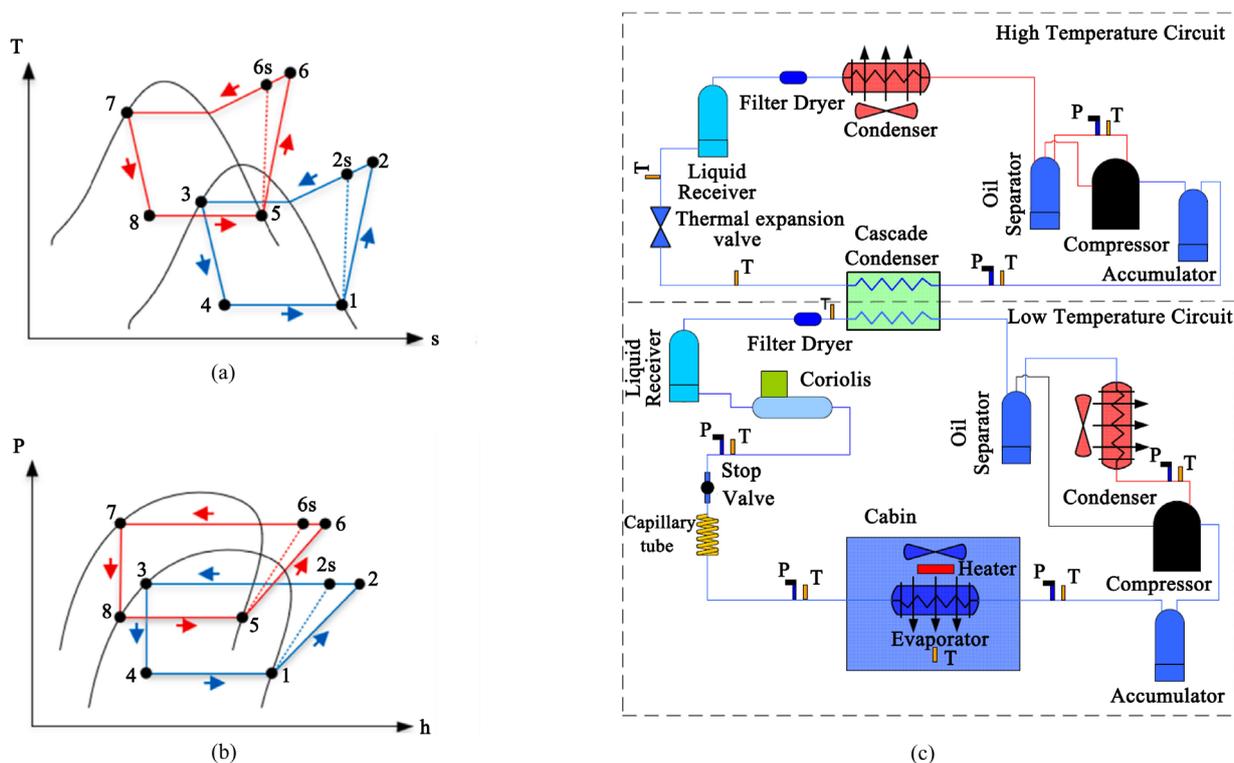

Figure 5. Cascade refrigeration cycle proposed as innovative refrigeration system for COVID-19 vaccines transportation and storage. (a), (b) CRS presented on T-s diagram and on p-h diagram, respectively, presented by Aktemur *et al.* [18], and (c) Line diagram for CRS with LTC and HTC, presented by Alhamid *et al.* [36].

3.4. Classification of Refrigerants

As can be seen on **Figure 5(b)**, the p-h diagrams dramatically influence the performance of the selected refrigerant, due to its thermodynamic properties. **Figure 6** depicts the methods can be used to classify the refrigerant either based on their chemical composition, as can be seen in **Figure 6(a)**, or based on their working temperature ranges, as can be seen in **Figure 6(b)**. The decision tree is shown in **Figure 6(a)**. depends on classifying the refrigerants into three groups; which are; the first group is HCFC group, such as R22, R23, R32, and R410A, the second group is HFC group, such as R123, R134a, and R407c, and the third group is Halogen free refrigerant either pure hydrocarbon refrigerant such as R50 (pure Methane), R170 (pure Ethane), and R290 (pure Propane), or Inorganic such as NH_3, and CO_2. The hydrocarbon refrigerant may have active mixtures as mixture hydrocarbon refrigerants such as Propane/Iso-butane, as can be seen in **Figure 6(a)**. On the other hand, **Figure 6(b)** classifies the refrigerant tested in the current article to achieve this research goals into three groups based on their working temperature ranges, which are high temperature ranges such as
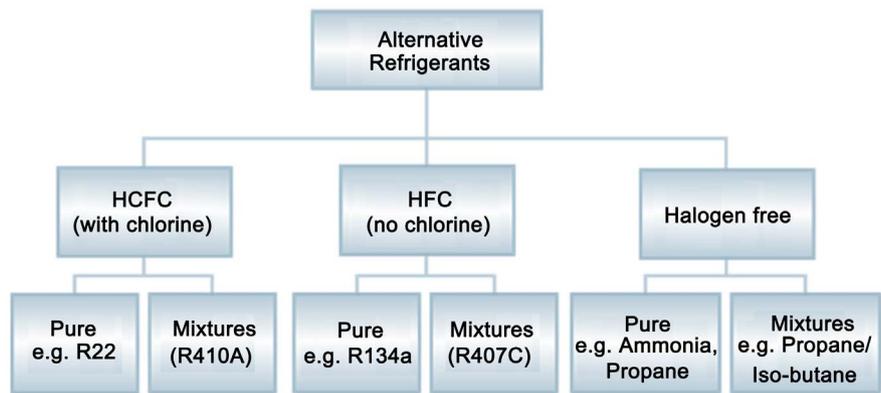
(a)
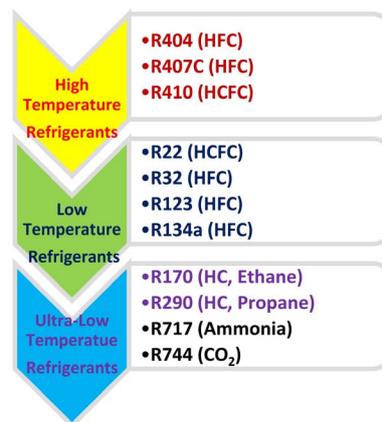
(b)

Figure 6. Refrigerant classification based on their chemical composition, and on their working temperature ranges. (a) based on their chemical composition, (b) based on their classification on their working temperature ranges, high, low, and ultra-low temperature ranges, which are numerically investigated in the current research.

R404, R407c, R410 and R507, Low temperature ranges such as R22 (used as base case only), R32, R123 and R134a, and Ultra Low temperature such as R170, and R290, as shown in Figure 6(b).

3.5. Research Methodology

The research methodology aims to present a thermodynamic analysis on both first law and second law of thermodynamics for proposed cascade refrigeration systems using coupling of refrigerants. This cascade refrigeration system (CRS) is proposed to cool down the evaporating temperature to store COVID-19 vaccines which may need keeping temperature either during transportation or during storage processes at low temperature reaches to −80°C. The numerically investigated cascade refrigeration machine consists of two refrigeration circuits, of low temperature cycle and high temperature cycle. The first refrigeration cycle is the high-temperature circuit (HTC) using several environmentally friendly refrigerants such as R22 as old reference commonly used since 1960s, R32, R123, R134a, R404, R407c, R410, and finally the most promising pure hydrocarbon refrigerant which is the propane namely as R290. On the other side, the second refrigeration cycle in the current study is the low temperature circuit (LTC) which uses also a pure hydrocarbon refrigerant namely Ethane (R170). Both systems are simulated to be interconnected to each other through the intermediate heat exchanger (also can be named cascade condenser), as can be seen in Figure 5(c). This intermediate heat exchanger is commonly used of the plate heat exchanger type. The different expansion devices of HTC and LTC are due to the fact that working pressures are not the same between the two circuits, as reported by Alhamid *et al.* [36]. The working principle between HTC and LTC are the same as a refrigeration cycle in general. The current research methodology focusses the interest on evaluating the commonly used parameters and metrics for both the energy analysis and the exergy analysis of the proposed CRS using different refrigerant pairs under different operating conditions by varying the intermediate temperature (T_{inter}) from −25°C to +5°C.

3.5.1. Energy Analysis Using the First Law of Thermodynamics

By applying the first law of thermodynamics, Energy analysis can be performed using the list of balance equations listed in Table 1. Most of these balance equations are commonly used by applying the first law of thermodynamics by several researches conducted on Energy analysis for cascade refrigeration systems, as presented by Ustaoglu *et al.* [5], Sun *et al.* [15], and Jain *et al.* [25]. To produce the results of this energy analysis study using the first law of thermodynamics the Coefficients of Performance (COPs) and Specific power consumptions (SPCs) in kW/TR can be numerically computed to compare between different opportunities of refrigerant pairing used under different operation conditions using different intermediate temperature (T_{inter}) from −25°C to +5°C. Table 1 depicts all these thermodynamics correlations and balance equations used to estimate the parameters and metrics of the first law of thermodynamics, using

Table 1. Balance Equations commonly used in Energy Analysis by applying first law analysis for the cascade refrigeration cycle and its system components, [5] [15] [25].

- Actual enthalpy at compressor outlet at LTC.

$$\eta_{\text{isen}} = \frac{h_{2s} - h_1}{h_2 - h_1}$$ Equation (1)

- Actual enthalpy at compressor outlet at HTC.

$$\eta_{\text{isen}} = \frac{h_{6s} - h_5}{h_6 - h_5}$$ Equation (2)

- Mass flow in LTC (heat balance over LTC evaporator)

$$\dot{m}_{\text{LTC}} = \frac{Q_{cc}}{h_1 - h_4}$$ Equation (3)

- Mass flow rate in HTC (heat balance over intermediate heat exchanger)

$$\dot{m}_{\text{HTC}} = \dot{m}_{\text{LTC}} * \frac{h_2 - h_3}{h_5 - h_8}$$ Equation (4)

- Work of LTC compressor (energy balance over LTC compressor)

$$W_{LTC,Comp} = m_{LTC} * (h_2 - h_1)$$ Equation (5)

- Work of HTC compressor (energy balance over HTC compressor)

$$W_{HTC,Comp} = m_{HTC} * (h_6 - h_5)$$ Equation (6)

- Heat transfer in intermediate heat exchanger (energy balance over entire LTC)

$$Q_{\text{int}} = Q_{cc} + W_{\text{LTC,Comp}}$$ Equation (7)

- Heat rejected by the upper cycle condenser (energy balance over entire HTC)

$$Q_{\text{rej}} = Q_{\text{int}} + W_{\text{HTC,Comp}}$$ Equation (8)

- Coefficient of performance (COP)

$$\text{COP}_{\text{LTC}} = \frac{Q_{cc}}{W_{\text{LTC,Comp}}}$$ Equation (9)

$$\text{COP}_{\text{HTC}} = \frac{Q_{\text{int}}}{W_{\text{HTC,Comp}}}$$ Equation (10)

$$\text{COP}_{\text{CRS}} = \frac{Q_{CC}}{W_{\text{HTC,Comp}} + W_{\text{LTC,Comp}}}$$ Equation (11)

the thermodynamic properties at different corners of the cascade refrigeration cycles numerically tested in the current research. The isentropic efficiencies (η_{isen}) are estimated in the current study using the definitions presented by Elakdhar *et al.* [37], and Brunin *et al.* [38].

3.5.2. Exergy Analysis Using the Second Law of Thermodynamics
By applying the second law of thermodynamics, Exergy Analysis can be executed using the list of equations listed in Table 2. Most of these balance equations are commonly used by applying the second law of thermodynamics by several researches conducted on Exergy analysis for cascade refrigeration systems, as presented by Ustaoglu *et al.* [5], Sun *et al.* [15], and Jain *et al.* [25].To perform

Table 2. Balance Equations commonly used in Exergy Analysis by applying the second law analysis on the cascade refrigeration cycle and its system components, [5] [15] [25].

- Exergy analysis over HTC, compressor

$$\dot{x}_{\text{HTC,Comp}} = T_a * \dot{m}_{\text{HTC}} \left(s_6 - s_5 \right)$$

Equation (12)

- Exergy analysis over HTC, condenser

$$\dot{x}_{\text{HT,cond}} = \left(T_a * \dot{m}_{\text{HTC}} * \left(s_7 - s_6 \right) \right) + \left(\dot{m}_{\text{HTC}} \left(h_6 - h_7 \right) \right)$$

Equation (13)

- Exergy analysis over HTC, evaporator

$$\dot{x}_{\text{HTC,evap}} = T_a * \dot{m}_{\text{HTC}} \left(s_8 - s_7 \right)$$

Equation (14)

- Exergy analysis over intermediate heat exchanger

$$\dot{x}_{\text{Intermediate,HEX}} = T_a * \left(\left(\dot{m}_{\text{LTC}} \left(h_3 - h_2 \right) \right) + \dot{m}_{\text{HTC}} * \left(s_5 - s_8 \right) \right)$$

Equation (15)

- Exergy analysis in LTC, comp.

$$\dot{x}_{\text{LTC,Comp}} = T_a * \dot{m}_{\text{LTC}} \left(s_2 - s_1 \right)$$

Equation (16)

- Exergy analysis over LTC, evaporator

$$\dot{x}_{\text{LTC,evap}} = T_a * \dot{m}_{\text{LTC}} \left(s_4 - s_3 \right)$$

Equation (17)

- Second law efficiency (Exergetic Efficiency)

$$\eta_{\text{II}} = \eta_{\text{exergetic}} = \frac{\dot{W}_{\text{LTC,Comp}} + \dot{W}_{\text{HTC,Comp}} - \dot{X}_{\text{Total}}}{\dot{W}_{\text{LTC,Comp}} + \dot{W}_{\text{HTC,Comp}}}$$

Equation (18)

Exergy analysis using the second law of thermodynamics the Exergetic Efficiencies can be generated to compare between different opportunities of refrigerant pairing used under different operation conditions using different intermediate temperature (T_{inter}) from −25°C to +5°C. Table 2 depicts the thermodynamics parameters and metrics of the second law of thermodynamics using the thermodynamic properties at different corners of the cascade refrigeration cycles presented in this article.

4. Results and Discussion

This section presents the results of Cascade Refrigeration Systems (CRSs) using several tested pairs of refrigerants, which are grouped into three groups of refrigerant pairs, (R32/R170, R123/R170 and R134a/R170), (R404/R170, R407c/R170, and R410/R170), and (R22/R170, and R290/R170) versus different intermediate temperature (T_{inter}) −25°C, −15°C, −5°C, and +5°C. The results are classified based on applying the first law of thermodynamics to estimate the coefficients of performance, discharge temperatures for both LTC and HTC, and the specific power consumptions (SPCs) in kW/TR, and by applying the second law of thermodynamics to evaluate the exergetic efficiencies (η_{II}) or ($\eta_{\text{exergetic}}$). The results of the first law analysis are generated using the governing (balance) equations listed in Table 1, however, the results of the second law analysis are evaluated using the governing (balance) equations listed in Table 2.

4.1. Results of the First Law Analysis

The results of the first law of thermodynamics for the coefficients of performance discharge temperatures for both LTC and HTC, $T_{discharge, 2}$ and $T_{discharge, 6}$, respectively, are presented in **Figures 7-9**. The discharge temperatures for both LTC and HTC, ($T_{discharge, 2}$ and $T_{discharge, 6}$), respectively, are plotted versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C. The results of the specific power consumptions (SPCs) in kW/TR are presented in **Figures 10-12**, and discussed in the next subsection 4.2. **Figure 7** shows the coefficients
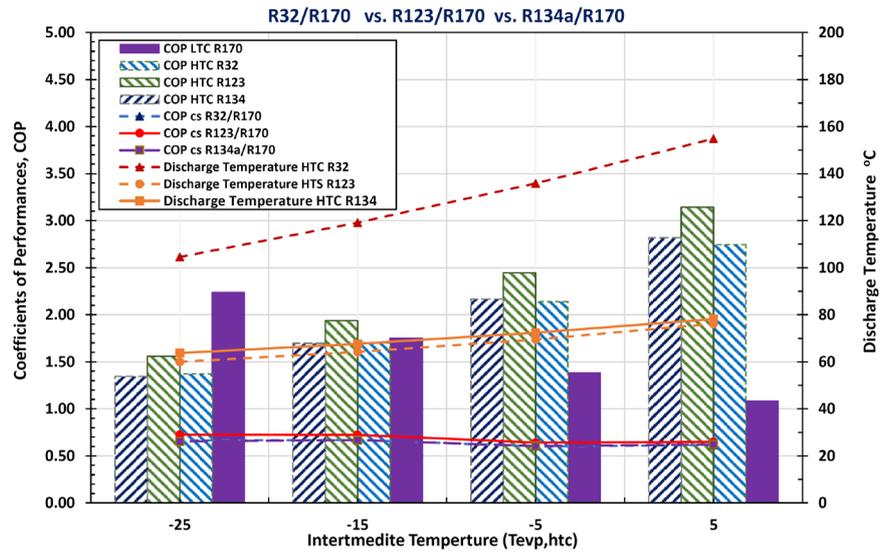
Figure 7. Coefficients of performance and discharges temperatures (T_6 at HTC) for three refrigerant pairs (R32/R170, R123/R170 and R134a/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.
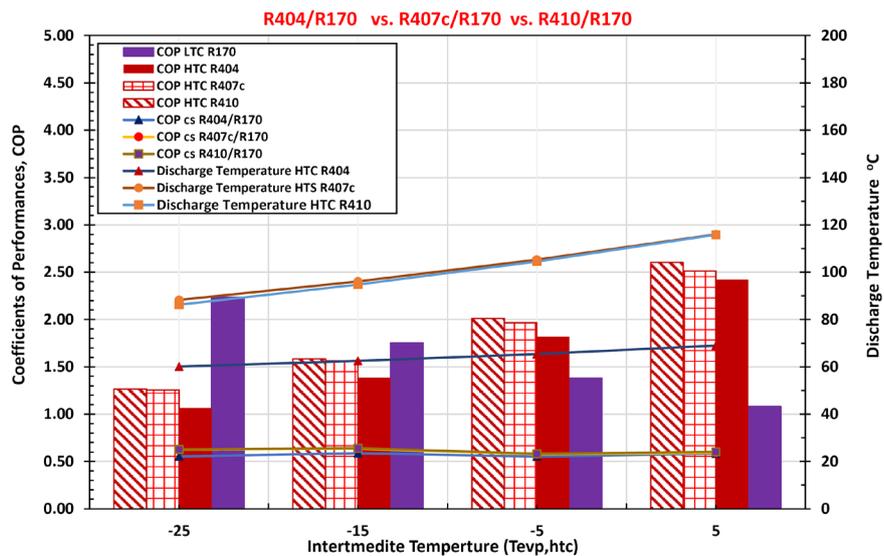
Figure 8. Coefficients of performance and discharges temperatures (T_6 at HTC) for three refrigerant pairs (R404/R170, R407c/R170, and R410/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.
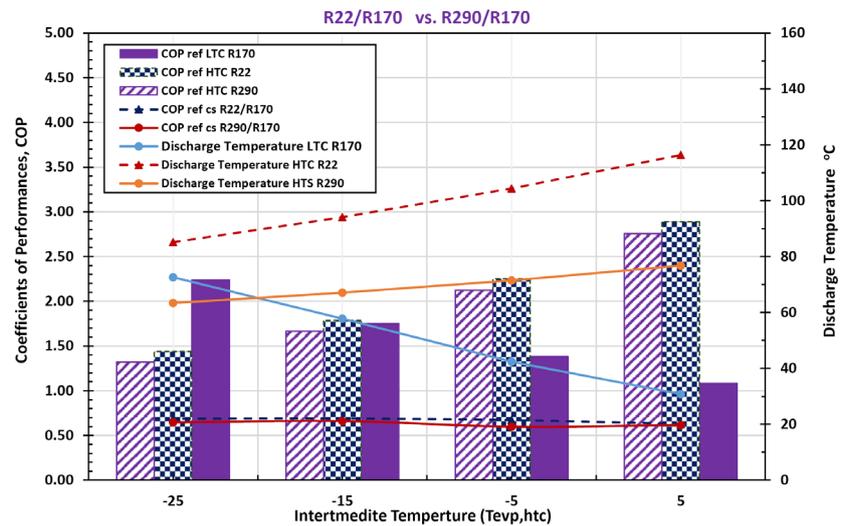
Figure 9. Coefficients of performance and discharges temperatures (T_2 at LTC and T_6 at HTC) for two refrigerant pairs (R22/R170, and R290/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.
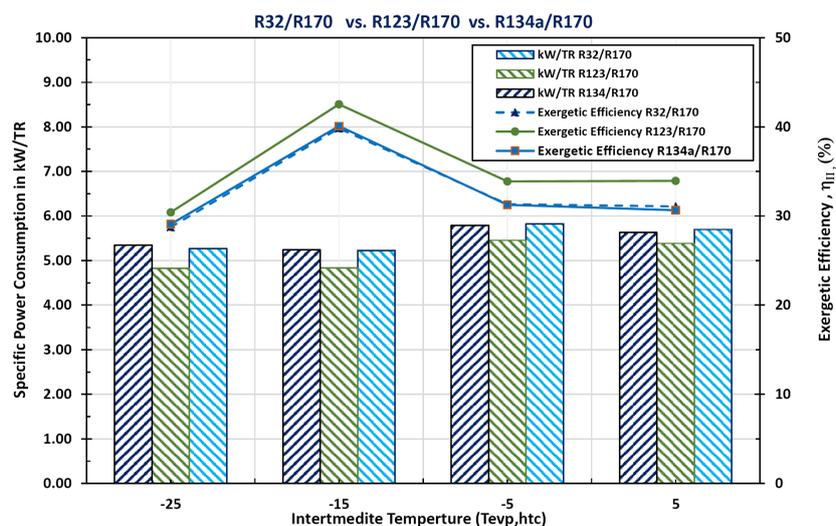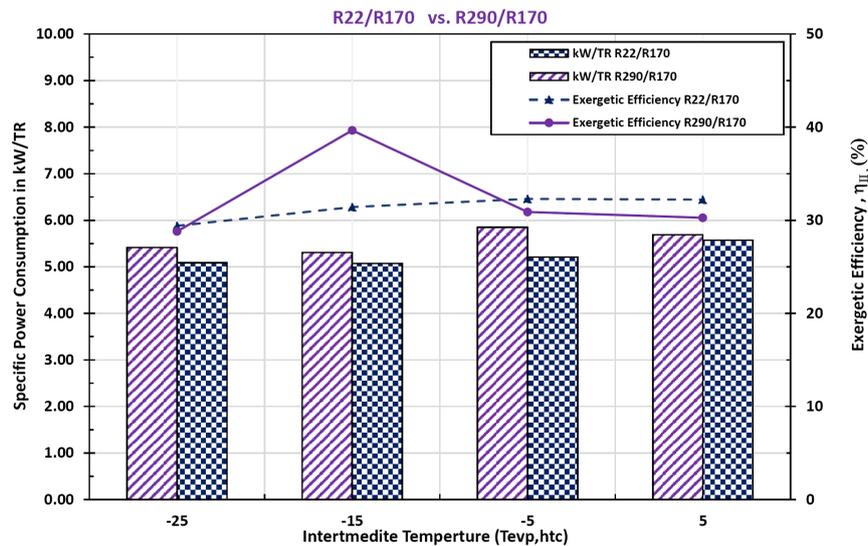

Figure 10. Specific power consumptions in kW/TR and Exergetic Efficiencies (η_{II}) for cascade refrigeration cycles consist of three refrigerant pairs (R32/R170, R123/R170 and R134a/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.

of performance and discharges temperatures (T_6 at HTC) for three refrigerant pairs (R32/R170, R123/R170 and R134a/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C. **Figure 8** displays the coefficients of performance and discharges temperatures (T_6 at HTC) for three refrigerant pairs (R404/R170, R407c/R170, and R410/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C. **Figure 9** shows the coefficients of performance and discharges temperatures (T_2 at LTC and T_6 at HTC) for two refrigerant pairs (R22/R170 and R290/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.
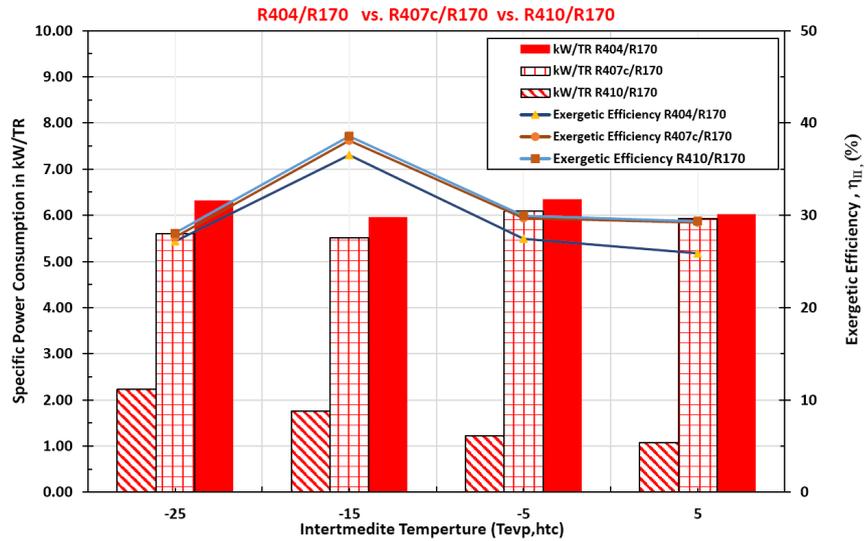
Figure 11. Specific power consumptions in kW/TR and Exergetic Efficiencies (η_{II}) for cascade refrigeration cycles consist of three refrigerant pairs (R404/R170, R407c/R170, and R410/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.

Figure 12. Specific power consumptions in kW/TR and exergetic efficiencies (η_{II}) for cascade refrigeration cycles consist of two refrigerant pairs (R22/R170, and R290/R170) versus different intermediate temperature (T_{inter}) −25˚C, −15˚C, −5˚C, and +5˚C.

4.2. Results of Specific Power Consumption (SPCs) in kW/TR

The current numerical analysis applied by the first law of thermodynamics gives that the SPCs for CRS applications in the COVID-19 vaccines transportation and storage is starts from 4.8 kW/TR up to 6 kW/TR. The results of specific power consumptions (SPCs) in kW/TR are presented in **Figures 10-12**, for the three sets of refrigerant pairs versus different intermediate temperature (T_{inter}) of −25˚C, −15˚C, −5˚C, and +5˚C. **Figure 9** depicts the SPCs per refrigerated tonnage in kW/TR for the refrigerant pairs (R32/R170, R123/R170 and R134a/R170)

versus different intermediate temperature (T_{inter}) of −25°C, −15°C, −5°C, and +5°C. Figure 9 shows that the pair R123/R170 gives the minimum SPC at 4.8 kW/TR, numerically recorded for T_{inter} = −10°C and −5°C. For other pairs, which contain high temperature range as HTC, as can be seen in Figure 6(b), such as R404/R170, R407c/R170, and R410/R170, the results depicted from Figure 11 give that all of them have the highest three values of the specific power consumption from 5.5 to 6.6 kW/TR, numerically recorded for all T_{inter} temperature range from −25°C to 5°C, as can be seen in Figure 11. Therefore, it will be recommended to not use these three pairs tested in this article objective either in the presence of the COVID-19 pandemic or after this pandemic. However, Figure 12 shows that the base case used for this current study, which is R22/R170 gives the minimum specific power consumption at 5.2 kW/TR, numerically recorded for T_{inter} = −5°C. Meanwhile, the highly recommended HC refrigerant pair in this article, which is depending on pure hydro carbon pair consists of both Ethane (R170) in LTC and Propane (R290) in HTC, gives almost constant and moderated value of the specific power consumption from 5.4 to 5.7 kW/TR, numerically recorded for all T_{inter}, as can be seen in Figure 12.

4.3. Results of Second Law Analysis

The exergetic efficiency ($\eta_{\text{exergetic}}$) is one of the most important parameters of the second law of thermodynamics. The current thermodynamic analysis gives that exergetic efficiencies ($\eta_{\text{exergetic}}$) for CRS applications in the COVID-19 vaccines transportation and storage starts from 25% up to 43%, as can be seen in Figures 10-12. Figure 10 depicts the $\eta_{\text{exergetic}}$ for the refrigerant pairs (R32/R170, R123/R170 and R134a/R170) versus different intermediate temperature (T_{inter}) of −25°C, −15°C, −5°C, and +5°C. Figure 11 shows the exergetic efficiency ($\eta_{\text{exergetic}}$) for the refrigerant pairs (R404/R170, R407c/R170 and R410/R170) versus different intermediate temperature (T_{inter}) of −25°C, −15°C, −5°C, and +5°C. Figure 12 shows the exergetic efficiency ($\eta_{\text{exergetic}}$) for two refrigerant pairs (R22/R170, and R290/R170) versus different intermediate temperature (T_{inter}) of −25°C, −15°C, −5°C, and +5°C. Figure 10 presents the pair R123/R170 gives that the $\eta_{\text{exergetic}}$ is recorded its numerically maximum value equal to 43%, at T_{inter} = −5°C. Figure 11 presents that results of the three pairs of high temperature range as HTC, which are R404/R170, R407c/R170, and R410/R170 as classified in Figure 6(b), give that all of them have the lowest three values of the $\eta_{\text{exergetic}}$ and its range starts from 25% to 32% and 39%, as can be seen in Figure 11. These findings confirm on the recommendations of applying the first law of thermodynamics by calculating the specific power consumption per refrigerated tonnage for CRS. Figure 12 shows that the base case used for this current study, which is R22/R170 gives a stable and relatively minimum values of the $\eta_{\text{exergetic}}$ which starts from 30% to 32% as recorded for T_{inter} = −25°C and −15°C. On the other side, the most promising pair in future few decades, which is proposed in current article as well R290/R170 gives almost constant and moderated value of the $\eta_{\text{exergetic}}$ of 30% at T_{inter} = −25°C, −15°C, and +5°C, however, it increases

rapidly to 40% at $T_{inter} = -5°C$, as can be seen in **Figure 12**.

These findings of both Energy and Exergy Analysis reveal the opportunity of using the pair consists of R290/R170 is highly recommended in these vaccine applications, besides, the unfeasibility of using some pairs in these transportation and storage applications such as R404/R170, R407c/R170, and R410/R170. The data and results presented in this article are very important and useful in providing the refrigeration solutions to containing the transportation and storage missions by production companies, and governments in many countries during the existing pandemic COVID-19.

5. Concluding Remarks and Recommendations

This article is dedicated to focus on the possibility of using cascade refrigeration for ultra-low temperature required for COVID-19 vaccines with focus the interest also on the opportunity of using different pairs of refrigerants included R170, as pure hydrocarbon refrigerant, in the low temperature cycle. The concluding remarks are listed as follows:

- Cascade Refrigeration system (CRS) can be efficiently used to provide the ultra-low temperatures (from −40°C to −80°C) to be used in both storage and transportation of COVID-19 vaccines with most of their types and specifications.
- Using R170 (Ethane) as pure hydrocarbon is promising free halogen refrigerant however, the precautionary measures shall be taken into consideration during utilizing R170 in the proposed CRSs either in trailers and tucks during transportation, or in cold stores inside clinics, hospital, and vaccination centers in remote villages.
- The efficient operation of CRS is dependent on both the low temperature to be reached and on the refrigerant pairs to be selected during CRS design stage.
- The influence of the selective cascade condenser temperature (intermediate temperature) can affect the coefficient of performance and it should be carefully selected during design stage regarding to the selected refrigerant pairs.

Finally, the recommendation for future work is to experimentally study the performance of these pairs or the most promising pairs to experimentally validate the current thermodynamic analysis to achieve the predicted isentropic efficiencies used to complete this current study, with those expected measured values which will be based on actual electrical power measurements. Meanwhile, the opportunities of using both compression and absorption cycles in one cascade refrigeration systems besides using solar energy for the absorption cycle, on higher temperature cycle, and electrical power for compression cycle, shall be carefully investigated either as thermodynamic analysis or experimentally measured using ready-made absorption machines with the smallest available capacity for experimental setup purposes. The recommendation for future work is to perform a complete 4Es analysis (Energy, Exergy, Economy, and Environment),

which will focus on certain designs for vaccines transportation and storage in future decades while using the highly recommended and promising refrigerant pair consists of purely hydrocarbon of both LTC and HTC, by using Ethane (R170) in LTC, and Propane (R290) in HTC, respectively.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Wood, J. (2021) Follow Two COVID-19 Vaccines on Two Very Different Cold Chain Journeys. *Forbes*, *Mitsubishi Heavy Industries*.
https://www.forbes.com/sites/mitsubishiheavyindustries/2021/03/25/follow-two-covid-19-vaccines-on-two-very-different-cold-chain-journeys-infographic/?sh=6598c2232796

[2] Biyani, V. (2021) COVID-19 Vaccine: Supply Chain Challenges. *Superprocure*.
https://www.superprocure.com/COVID-19-vaccine-supply-chain-challenges

[3] Kaul, R. (2021) India News, Transportation to Jabs: Centre Outlines Covid Vaccination Plan. *Hindustan Times*.
https://www.hindustantimes.com/india-news/transportation-to-jabs-centre-outlines-covid-vaccination-plan/story-ia3KVh6KjtuX03HCeSEWSI.html

[4] Wang, H., Song, Y. and Cao, F. (2020) Experimental Investigation on the Pull-Down Performance of a −80 ˚C Ultra-Low Temperature Freezer. *International Journal of Refrigeration*, **119**, 1-10. https://doi.org/10.1016/j.ijrefrig.2020.04.030

[5] Ustaoglu, A., Kursuncu, B., Alptekin, M. and Gok, M.S. (2020) Performance Optimization and Parametric Evaluation of the Cascade Vapor Compression Refrigeration Cycle Using Taguchi and ANOVA Methods. *Applied Thermal Engineering*, **180**, Article ID: 115816. https://doi.org/10.1016/j.applthermaleng.2020.115816

[6] Rui, S., Zhang, H., Zhang, B. and Wen, D. (2016) Experimental Investigation of the Performance of a Single-Stage Auto-Cascade Refrigerator. *Heat and Mass Transfer*, **52**, 11-20. https://doi.org/10.1007/s00231-015-1577-4

[7] Roy, R. and Mandal, B.K. (2020) Thermo-Economic Analysis and Multi-Objective Optimization of Vapour Cascade Refrigeration System Using Different Refrigerant Combinations: A Comparative Study. *Journal of Thermal Analysis and Calorimetry*, **139**, 3247-3261. https://doi.org/10.1007/s10973-019-08710-x

[8] Roy, R. and Mandal, B.K. (2019) Energetic and Exergetic Performance Comparison of Cascade Refrigeration System Using R170-R161 and R41-R404A as Refrigerant Pairs. *Heat and Mass Transfer*, **55**, 723-731.
https://doi.org/10.1007/s00231-018-2455-7

[9] Gong, M., Sun, Z., Wu, J., Zhang, Y., Meng, C. and Zhou, Y. (2009) Performance of R170 Mixtures as Refrigerants for Refrigeration at L 80 ˚C Temperature Range. *International Journal of Refrigeration*, **32**, 892-900.
https://doi.org/10.1016/j.ijrefrig.2008.11.007

[10] Zou, X., Gong, M.Q., Chen, G.F., Sun, Z.H., Zhang, Y. and Wu, J.F. (2010) Experimental Study on Saturated Flow Boiling Heat Transfer of R170/R290 Mixtures in a Horizontal Tube. *International Journal of Refrigeration*, **33**, 371-380.
https://doi.org/10.1016/j.ijrefrig.2009.10.013

[11] Zhuang, X.R., Gong, M.Q., Zou, X., Chen, G.F. and Wu, J.F. (2016) Experimental Investigation on Flow Condensation Heat Transfer and Pressure Drop of R170 in a Horizontal Tube. *International Journal of Refrigeration*, **66**, 105-120.
https://doi.org/10.1016/j.ijrefrig.2016.02.010

[12] Chen, Q., Zhou, L., Yan, G. and Yu, J. (2019) Theoretical Investigation on the Performance of a Modified Refrigeration Cycle with R170/R290 for Freezers Application. *International Journal of Refrigeration*, **104**, 282-290.
https://doi.org/10.1016/j.ijrefrig.2019.05.037

[13] Park, K. and Jung, D. (2009) Performance of Heat Pumps Charged with R170/R290 Mixture. *Applied Energy*, **86**, 2598-2603.
https://doi.org/10.1016/j.apenergy.2009.04.009

[14] Sun, Z., Liang, Y., Liu, S., Ji, W., Zang, R., Liang, R. and Guo, Z. (2016) Comparative Analysis of Thermodynamic Performance of a Cascade Refrigeration System for Refrigerant Couples R41/R404A and R23/R404A. *Applied Energy*, **184**, 19-25.
https://doi.org/10.1016/j.apenergy.2016.10.014

[15] Sun, Z., Wang, Q., Xie, Z., Liu, S. and Su, D. (2019) Energy and Exergy Analysis of Low GWP Refrigerants in Cascade Refrigeration System. *Energy*, **170**, 1170-1180.
https://doi.org/10.1016/j.energy.2018.12.055

[16] Nawaz, K., Shen, B., Elatar, A., Baxter, V. and Abdelaziz, O. (2017) R290 (Propane) and R600a (Isobutane) as Natural Refrigerants for Residential Heat Pump Water Heaters. *Applied Thermal Engineering*, **127**, 870-883.
https://doi.org/10.1016/j.applthermaleng.2017.08.080

[17] Liu, Y. and Yu, J. (2019) Performance Evaluation of an Ejector Subcooling Refrigeration Cycle with Zeotropic Mixture R290/R170 for Low-Temperature Freezer Applications. *Applied Thermal Engineering*, **161**, Article ID: 114128.
https://doi.org/10.1016/j.applthermaleng.2019.114128

[18] Aktemur, C., Ozturk, I.T. and Cimsit, C. (2021) Comparative Energy and Exergy Analysis of a Subcritical Cascade Refrigeration System Using Low Global Warming Potential Refrigerants. *Applied Thermal Engineering*, **184**, Article ID: 116254.
https://doi.org/10.1016/j.applthermaleng.2020.116254

[19] Turgut, M.S. and Turgut, O.E. (2019) Comparative Investigation and Multi Objective Design Optimization of R744/R717, R744/R134a and R744/R1234yf Cascade Refrigeration Systems. *Heat and Mass Transfer*, **55**, 445-465.
https://doi.org/10.1007/s00231-018-2435-y

[20] Das, I. and Samanta, S. (2021) Comparative Energetic and Exergetic Analyses of a Cascade Refrigeration System Pairing R744 with R134a, R717, R1234yf, R600, R1234ze, R290. Lecture Notes in Mechanical Engineering. Springer, Singapore.
https://doi.org/10.1007/978-981-15-6360-7_20

[21] Xie, Y., Liu, C., Lun, L. and Zhang, X. (2008) Use of R290/R170 in Lieu of R22/R23 in Cascade Refrigeration Cycle. *International Refrigeration and Air Conditioning Conference*, Purdue Indiana, 14-17 July 2008, Paper 939, 1-7.

[22] Wang, Q., Cui, K., Sun, T.F., Chen, F.S. and Chen, G.M. (2010) Performance of a Single-Stage Linde-Hampson Refrigerator Operating with Binary Refrigerants at the Temperature Level of −60 ˚C. *Journal of Zhejiang University: Science A*, **11**, 115-127. https://doi.org/10.1631/jzus.A0900208

[23] Fatouh, M. and El Kafafy, M. (2006) Experimental Evaluation of a Domestic Refrigerator Working with LPG. *Applied Thermal Engineering*, **26**, 1593-1603.
https://doi.org/10.1016/j.applthermaleng.2005.11.026

[24] Pan, M., Zhao, H., Liang, D., Zhu, Y., Liang, Y. and Bao, G. (2020) A Review of the

Cascade Refrigeration System. *Energies*, **13**, 2254.
https://doi.org/10.3390/en13092254

[25] Jain, V., Kachhwaha, S.S. and Sachdeva, G. (2013) Thermodynamic Performance Analysis of a Vapor Compression—Absorption Cascaded Refrigeration System. *Energy Conversion and Management*, **75**, 685-700.
https://doi.org/10.1016/j.enconman.2013.08.024

[26] Cheng, Z., Wang, B., Shi, W. and Li, X. (2020) Performance Evaluation of Novel Double Internal Auto-Cascade Two-Stage Compression System Using Refrigerant Mixtures. *Applied Thermal Engineering*, **168**, Article ID: 114898.
https://doi.org/10.1016/j.applthermaleng.2020.114898

[27] Dixit, M., Arora, A. and Kaushik, S.C. (2017) Energy, Exergy, Environment and Economic Analyses and Optimization of Two-Stage Absorption-Compression Combined Refrigeration System. *Clean Technologies and Environmental Policy*, **19**, 2215-2229. https://doi.org/10.1007/s10098-017-1404-3

[28] Bulula, N., Mwiru, D.P., Swalehe, O. and Thomas, A. (2020) Vaccine Storage and Distribution between Expanded Program on Immunization and Medical Store Department in Tanzania: A Cost-Minimization Analysis. *Vaccine*, **38**, 8130-8135.
https://doi.org/10.1016/j.vaccine.2020.10.088

[29] Zhao, Y., Zhang, X., Xu, X. and Zhang, S. (2020) Development of Composite Phase Change Cold Storage Material and Its Application in Vaccine Cold Storage Equipment. *Journal of Energy Storage*, **30**, Article ID: 101455.
https://doi.org/10.1016/j.est.2020.101455

[30] Holm, M.R. and Poland, G.A. (2021) Critical Aspects of Packaging, Storage, Preparation, and Administration of mRNA and Adenovirus-Vectored COVID-19 Vaccines for Optimal Efficacy. *Vaccine*, **39**, 457-459.
https://doi.org/10.1016/j.vaccine.2020.12.017

[31] Mouneer, T.A. (2021) Sustainable Development Importance in Higher Education for Occupational Health and Safety Using Egypt Vision 2030 under COVID-19 Pandemic. *Journal of Geoscience and Environment Protection*, **9**, 74-112.
https://doi.org/10.4236/gep.2021.94006

[32] Shervani, Z., Khan, I., Khan, T. and Qazi, U.Y. (2020) COVID-19 Vaccine. *Advances in Infectious Diseases*, **10**, 195-210. https://doi.org/10.4236/aid.2020.103020

[33] Williamson, L. (2021) Covid: The Challenge in Speeding Up France's Vaccination Drive. BBC Paris Correspondent.
https://www.bbc.com/news/world-africa-55975052

[34] McCarthy, N. (2020) COVID-19 Pandemic: The Cost per Jab of COVID-19 Vaccine Candidates. Statista.
https://www.statista.com/chart/23658/reported-cost-per-dose-of-COVID-19-vaccines

[35] AVAC (2020) Leveraging the HIV Vaccine Enterprise for COVID-19 Vaccine Research. AVAC.
https://www.avac.org/infographic/leveraging-hiv-vaccine-enterprise-COVID-19-vaccine-research

[36] Alhamid, M.I., Nasruddin, Darwin, R.B.S. and Lubis, A. (2013) Characteristics and Cop Cascade Refrigeration System Using Hydrocarbon Refrigerant (Propane, Ethane and CO_2) at Low Temperature Circuit (LTC). *International Journal of Technology*, **4**, 112-120. https://doi.org/10.14716/ijtech.v4i2.125

[37] Elakdhar, M., Nehdi, E. and Kairouani, L. (2007) Analysis of a Compression/Ejection Cycle for Domestic Refrigeration. *Industrial & Engineering Chemistry Research*,

46, 4639-4644. https://doi.org/10.1021/ie070377e

[38] Brunin, O., Feidt, M. and Hivet, B. (1997) Comparison of the Working Domains of Some Compression Heat Pumps and a Compression-Absorption Heat Pump. *International Journal of Refrigeration*, **20**, 308-318.
https://doi.org/10.1016/S0140-7007(97)00025-X

Nomenclature

COP_{CRS}	coefficient of performance for cascade refrigeration cycle	(--)
COP_{HTC}	coefficient of performance for gas driven chiller	(--)
COP_{LTC}	coefficient of performance for hybrid chiller plant	(--)
h	enthalpy	(J/kg)
m_{HTC}	Refrigerant mass flow rate at high temperature cycle	(kg/s)
m_{LTC}	Refrigerant mass flow rate at low temperature cycle	(kg/s)
p	pressure (kPa)	
Q_{cc}	cooling capacity at evaporator of low temperature cycle	(kW)
Q_{inter}	Heat rejected in intermediate heat exchanger	(kW)
s	entropy	(J/kg·K)
SPC	Specific Power Consumption per Refrigerated Tonnage	(kW/TR)
T	temperature	(˚C)
T_{cond}	Condensing temperature	(˚C)
T_{evap}	Evaporating temperature	(˚C)
T_{inter}	Intermediate temperature at cascade heat exchanger	(˚C)
$W_{HTC, Comp}$	work of compressor in high temperature cycle	(kW)
$W_{LTC, Comp}$	work of compressor in law temperature cycle	(kW)
x_{Total}	total exergy loss	(kW)
x	exergy loss	(kW)

Greek Symbol

$\eta_{exergetic}$	exergetic efficiency	(%)
η_{II}	second law efficiency	(%)
η_{isen}	isentropic efficiency	(%)

Subscripts

cc	cooling capacity
comp	compressor
cond	condenser/condensing
CRS	cascade refrigeration system
evap	evaporator/evaporating
HTC	high temperature cycle
LTC	low temperature cycle
inter	Intermediate
s	Isentropic process state
1, 2, 3, 4	state points of LTC in Figure 6.
5, 6, 7, 8	state points of HTC in Figure 6.

Abbreviations

CO_2	Carbon Dioxide
COP	coefficient of performance
COVID	Corona Virus Dieses

CRS Cascade refrigeration system
HC Hydro Carbon
HCFH Hydro Cluoro Fluoro Carbon
HEX Heat Exchanger
HFC Hydro Fluoro Carbon
Li-Br Lithium Bromide
NH$_3$ Ammonia
SPC Specific Power Consumption
TR refrigeration tonnage
USD United States Dollar