Diabetes Mellitus: Indigenous Solution to the 21st Century Epidemic

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Abstract - Diabetes mellitus is a generic term given to a group of metabolic diseases which cause high blood sugar in the patient. Research has associated diabetes with heart ailments and various disabilities, making it even deadlier and therefore a more urgent issue to be dealt with. In the Indian context, the fight against diabetes gets further complicated since it is a nation of haves and have-nots, with the rural areas taking the major brunt of poor infrastructure. Insulin, the primary medication to diabetes has to be stored in cold conditions, which to a large extent is not possible in the poorly electrified Indian villages. The absence of a cold chain infrastructure has left a glaring void in the Indian health sector, which the authors of this paper seek to partially fill through an economically feasible heat exchanger, especially tailored for the rural areas. The paper discusses the design of the aforementioned prototype, the materials used for its constructions and does a comparative analysis of the coolants, namely urea and ammonium chloride; a commercial design is also proposed for insulin storage.

Keywords: Rural, India, Diabetes, Insulin, Urea, Ammonium Chloride, Coolant, Endothermic reaction

I. STATUS QUO OF RURAL INDIA

India has come a long way since its independence 67 years ago; although the world's largest democracy has grown at an average rate of 8% in the last decade and figures as a future superpower, subpar social indicators besmirch its reputation. India fares abysmally poor in the health sector, a key parameter of human resource development. India can be best described as an oasis of affluence in a vast desert of poverty, a country where growth is concentrated in urbanized modern centers while the sister Indian villages are plagued with abject poverty and poor infrastructure. A town is considered rural on different sets of parameters; the Planning Commission views a region rural when the maximum population is 15,000 while the National Sample Survey Organization (NSSO) defines it as an area with population density of up to 400 per sq. km with at least 75% of male working population engaged in agriculture and allied activities. [1]

Electricity is extremely crucial to human resource development [2] and although intense public demand for access to electricity translated into political imperative and led to the connection of over 80% of the 550,000 villages to the national grid, the challenge of securing a regular power supply still persists; reasons ranging from high capital cost of transmission lines and imported electricity generation equipment [3] to high transmission & distribution losses along with the extraneous costs of centralized power production [4] have been attributed to the erratic supply with power cuts now an accepted baggage. In addition to the socio-economic challenges of electricity usage for rural areas, the production of electricity in India is 70% coal-derived, making it a significant contributor to greenhouse gas emissions. Therefore indigenous energy sources become an environmentally, economically and socially beneficial model for the rural areas by default.

II. DIABETES MELLITUS & INSULIN MEDICATION

Diabetes is one of the major health epidemics that the 21st century world faces, with India leading the global top ten in terms of the highest number of people with diabetes with a prevailing figure of 40.9 million. Diabetes is deadly. Once thought of as an "elderly" disease, diabetes has risen to epidemic levels in people of working age, particularly in developing countries. It kills approximately 3.8 million people per year, similar in magnitude to HIV/AIDS. [5] Produced by pancreatic beta cells, Insulin is a peptide hormone comprising of a protein chain of 51 amino acids and is crucial for metabolizing carbohydrates in the body. [6] A slight complication in insulin production can have widespread ramifications on tissues and organs; failure of insulin production leads to a condition called diabetes mellitus which has three major types [7]:

a) *Type 1 diabetes*- production of insulin from the pancreatic beta cells is negligible and patients are treated with external insulin injected subcutaneously.

b) *Type 2 diabetes/insulin resistance*- demands of insulin are unmet by the pancreatic beta cells and patients are given externally supplied insulin to reduce the blood sugar levels.

c) *Gestational diabetes*- a minor variant of diabetes found to occur for the first time during pregnancy due to a shortage of insulin. Although most women are able to control it with proper diet and physical activity, some women are required to take insulin.

Medicines for diabetes can be taken in various forms depending on the way in which insulin is injected; insulin injection and insulin jet injector are the most popular methods with insulin pump, insulin patch and insulin infuser being other alternatives. Efficiency of insulin is temperature dependent with insulin losing its potency and biological activity at extreme temperatures. Therefore insulin is never frozen, or exposed to a combination of high temperatures and excessive vibration. [8,9] Unused cartridges, pens and bottles of insulin, generally last till the expiration date when stored between 36°F and 46°F in the refrigerator while open insulin cartridges and pens can be kept at room temperature, i.e., between 56°F and 80°F. [10] A major health challenge for natives of tropical and subtropical regions is the "cold chain," the need to refrigerate temperature-sensitive drugs including insulin inter alia. [11]

We propose an economical prototype tailored to rural needs for insulin storage, targeting the transportation segment of the aforementioned cold chain, in the hope of strengthening the Indian public health infrastructure.

III. LITERATURE REVIEW

i. Heat exchanger

The basic purpose of a heat exchanger is to facilitate heat exchange between two fluids in an efficient manner. The primary fluid can either be heated by external utilities such as steam, combustion gas and electricity or can be cooled by cooling water and refrigeration. Feasibility of a heat exchanger is that heat can only be transferred from a higher temp to a lower one, meaning the higher temperature cooling curve and lower temperature heating curves cannot intersect, i.e., an establishment of thermal equilibrium when the temperatures of both the fluids become equal. [12] Design parameters of a heat exchanger include size or compactness, heat transfer rate and heat duty, i.e., the capacity in terms of heat energy transferred per unit time.

Reactions (or processes) that cool the surroundings by absorbing energy in the form of heat are characterized as endothermic or endergonic reactions. In physical sciences, namely, chemistry, endothermic reactions involve the conversion of thermal energy (heat) into chemical bond energy. Since the heat is placed on the reactants side, a fluid's temp. can be lowered if the coolant in the heat exchanger tube undergoes an endothermic reaction. Heat exchangers are extensively used in chemical industries, especially the pharmaceutical sector.

ii. Coolant

Table 1: Comparative analysis of the proposed coolants

Property	Ammonium Chloride	Urea
Molecular formula	NH_4Cl	CH_4N_2O
Molar mass	53.491 g/mol	60.06 g mol^{-1}
Odor	Odorless	odorless
Density	1.5274 g/cm^3	1.32 g/cm^3
Melting point	338 °C (decomposes)	133–135 °C
Boiling point	520 °C	150°C (Decomposes)
Solubility@ 20 °C	372 g/L	107.9 g/100 ml
Appearance	White solid; hygroscopic	White solid; hygroscopic
Flash point	Non-flammable	Non-flammable
Acidity (pK_a) / Basicity (pK_b)	Acidic (9.24)	Basic(0.18)

III. INSULIN

Table 2: Properties of insulin, "Novomix 30 –Penfill"

Property	Description
Appearance	Suspension used for injections is white, aqueous & cloudy
Storage	Storage is between 2°C-8°C for unopened penfill while it is below 30°C during use or when carried as a spare
Shelf Life	2 years for unopened penfill and up to 4 weeks during use or when carried as a spare.
Ingredients	*Active*: soluble insulin aspart and protamine – crystallized insulin aspart (100 U/Ml) in 30:70 ratio. *Inactive*: mannitol, phenol, meta-cresol, $ZnCl_2$, NaCl, NaOH, dibasic sodium phosphate dihydrate, protamine sulfate, hydrochloric acid and water for injections.
Working	Insulin protamine crystals are absorbed more slowly than insulin aspart, thus lowering the blood glucose level for a prolonged time. When mixed together, they start working within 10-15 min. and produce maximum effect between 1-4 hrs.
Target Groups	Older people (>65 yrs), paediatric population including adolescents & children above 10 yrs age. Not advised for people allergic to insulin aspart or having a diabetic coma.
Side Effects	Adverse reactions might arise due to pharmacological effect of product, namely, metabolism, immunity, eye and skin tissue disorders. Excess dose may lead to hypoglycaemia (low blood sugar level) while under dose may cause hyperglycaemia (high blood sugar level).

IV. PROTOTYPE

Table 3: Salient features of Prototype Design

Component	Description	Function	Cost
Vessel	Normal flat base vessel made of any material easily available in market. Although plastic is preferred, for experimentation a copper vessel is used.	It holds the water that is required to be cooled along with the cooling apparatus	Rs. 55
Chamber lid	Thick thermocol layer having a diameter slightly larger than that of the vessel is tightly fitted on the vessel. The layer is detachable for filling the vessel.	It holds the reaction candles and provides an insulated covering for the vessel	Rs 20
Reaction candles	Copper/Steel glass with flat base and open top are fitted into the chamber lid; external fins can be installed for increased heat transfer area	They contain the coolant and provide volume for the endothermic reaction of the coolant to take place with water	Rs. 25 per steel glass
Candle lid	The lids are made of thick thermocol and are tightly fitted on top of the candles. The lids are detachable for the loading and unloading of the coolant.	The lids provide insulation for the candle tops and have three holes each to felicitate the release of ammonia (which is highly improbable) to avoid pressure build up in the chamber.	Included in the chamber lid cost
Coolant	The coolant which is in powdered form is first put in the reaction candles and then water is added in specified amounts.	The coolant is responsible for the main cooling of the water in the vessel.	NH_4Cl: Rs.20 /Kg $(NH_2)_2CO$: Rs5.6/Kg
Earthen, fodder and jute bag insulation	Baked mud /clay is molded around the vessel while the fodder is stuffed over it. The Gunny Sack bag is stitched over the insulation layers.	Clay and fodder increase the insulation and prevent flow of heat from ambient atmosphere to the vessel. The jute bag reinforces the insulation and contains the mud and the fodder layers applied around the vessel.	Clay and fodder are free; can be obtained from natural sources. Jute costs Rs. 2.5 (approx.)
a) Total cost with ammonium chloride as the coolant b) Total cost with urea as the coolant			Rs. 105.5 Rs. 103.2

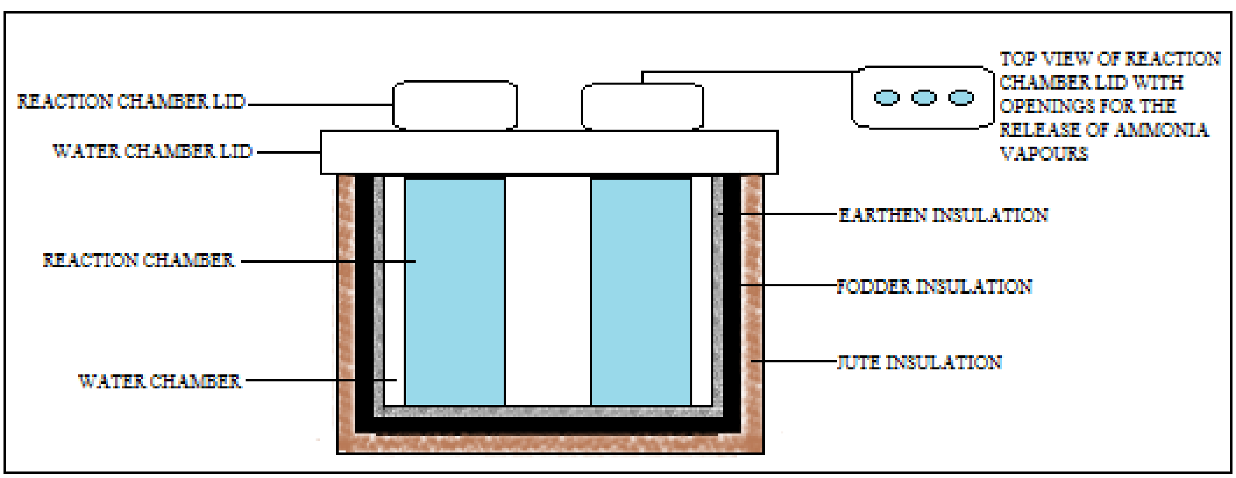


Figure 1: Schematic diagram of Prototype

V. EXPERIMENTATION

i. Methodology

The temperatures of insulin in the cartridges and of tap water were measured by using a thermometer. Specific amounts of urea and ammonium chloride were weighed using a digital balance.

The vessel was then filled with 500ml of water containing the insulin cartridges and the chamber lid holding the reaction candles, was placed on top. The reaction candles were filled with 200ml of water each along with ammonium chloride. The mixture was stirred and the candle lids quickly placed to cover the candles. The clay and jute insulation prevented the flow of heat to the environment, enabling us to measure steady temperature values of the water in the vessel and reaction candles, and of insulin in the cartridges at decided time intervals. The effect of coolant was evaluated in the subsequent test runs by replacing ammonium chloride with urea. To achieve robustness in the test runs, the quantity of the water in the vessel was changed from 500 ml to 300ml and the water was preheated to negotiate higher temps.

ii. Calculations

5g of ammonium chloride (NH_4Cl) dissolves completely in100cm^3 of water, to produce cooling. Let the resultant temperature difference (ΔT) be x$^\circ$C.

On solving, $\Delta H_1 = Cp*m*\Delta T$ where specific heat capacity of water (C_p) is 4.18 kJ kg^{-1} $^\circ$C^{-1} and mass of water = vol.*density=0.1*1=0.1kg;

we get, $\Delta H_1 = 0.418*x$ kJ

x was experimentally found as -3.3°C

$\Delta H_1 = 1.38$ kJ

Using proportionality to find the enthalpy change for 1 mole of NH_4Cl (i.e. 53.5g): ΔH_1 =17.7 kJ mol^{-1}

Similarly for dissolution of 5g urea (NH_2CONH_2) in100cm^3 of water, resulting in a temperature difference of 2.75°C,

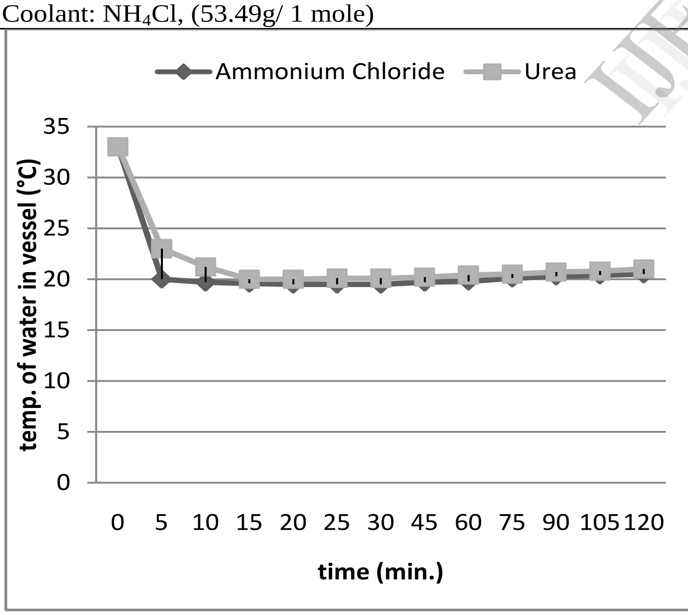
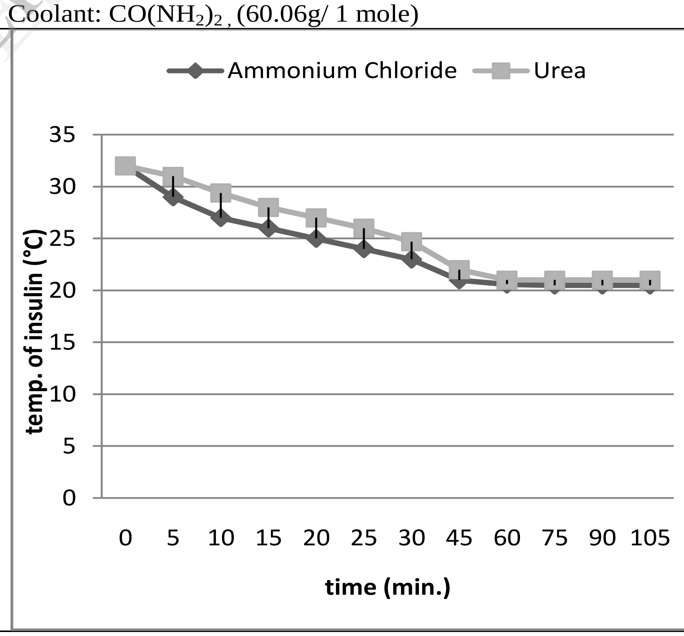
$\Delta H_2 = Cp*m*\Delta T = 0.418*x$ kJ = 1.15 kJ

Using proportionality to find the enthalpy change for 1 mole of urea (i.e. 60.06 g): ΔH_2 =13.8kJ mol^{-1}

It is evident from the above calculations that the heat of solution of ammonium chloride is greater than that of urea for the same amount of water at the same prevailing conditions.

III. OBSERVATION

Table 4: Graphs delineating the variation of candle temperature with time

<table>
<tr><td colspan="2">a) Water in vessel:500ml; Water in candle:200ml each</td></tr>
<tr><td>Coolant: NH_4Cl, (53.49g/ 1 mole)</td><td>Coolant: $CO(NH_2)_2$, (60.06g/ 1 mole)</td></tr>
<tr><td>
</td><td>
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<tr><td colspan="2">b) Water in vessel:300ml; Water in candle:200ml each</td></tr>
<tr><td>Coolant: NH_4Cl, (53.49g/ 1 mole)</td><td>Coolant: $CO(NH_2)_2$, (60.06g/ 1 mole)</td></tr>
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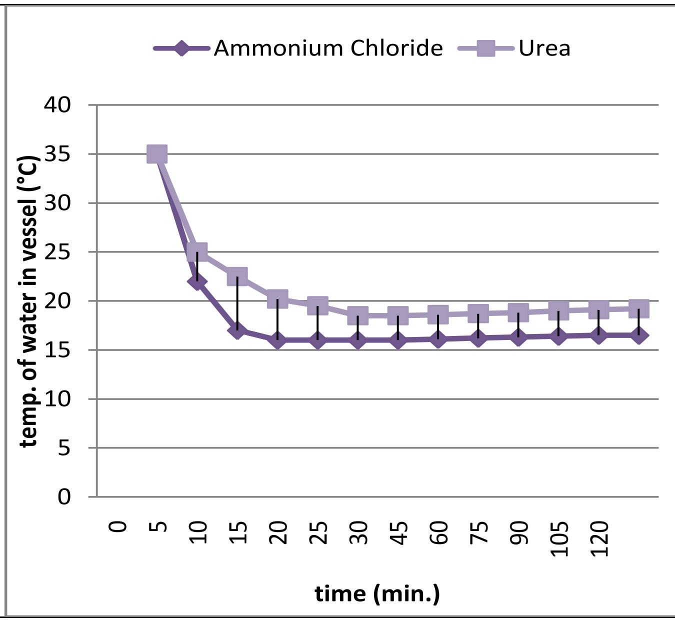
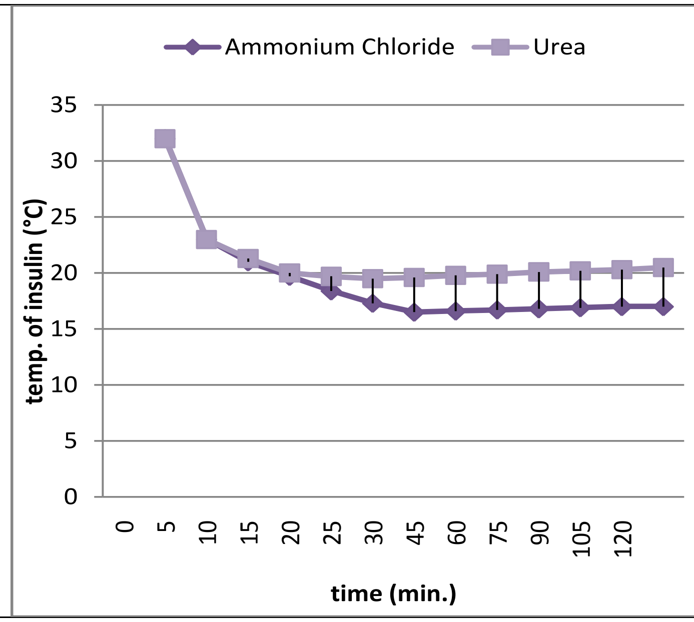
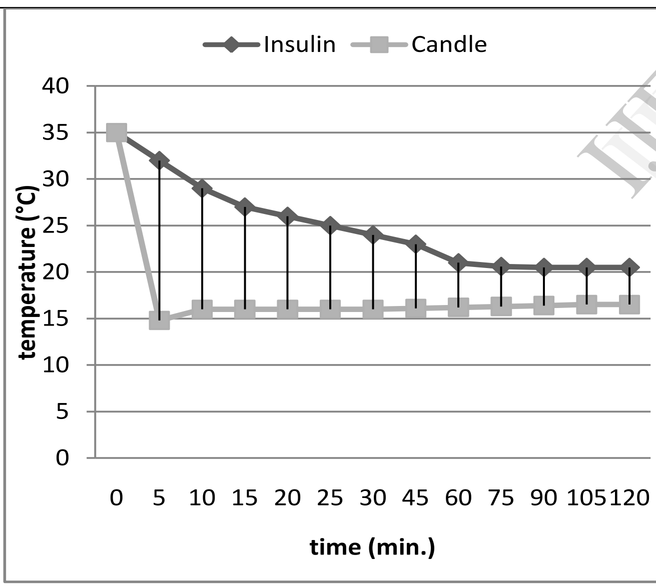
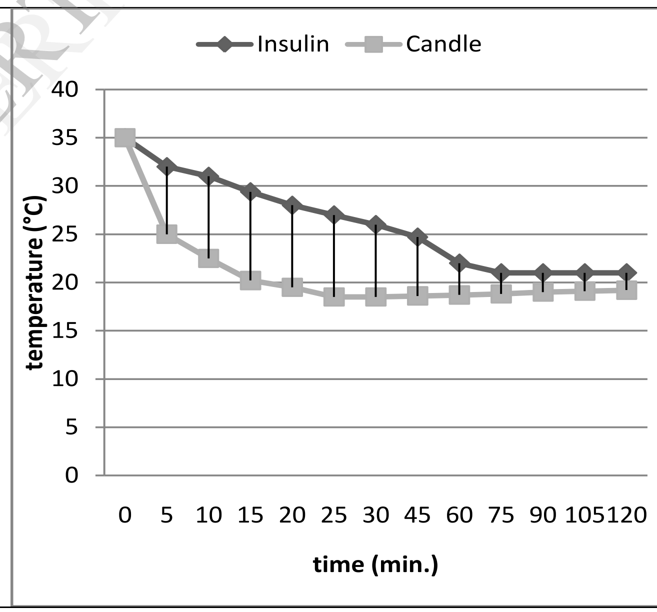
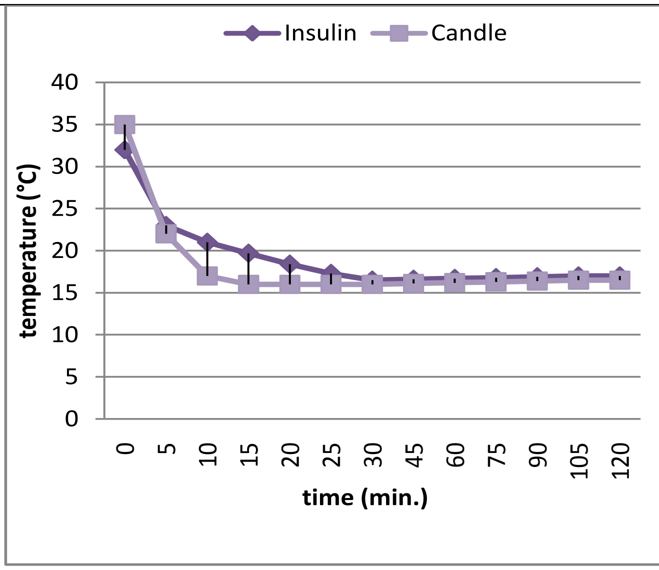
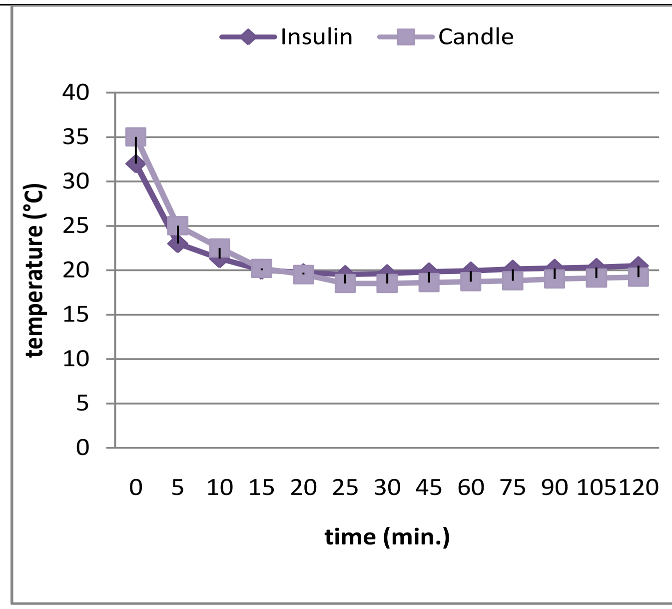
	

Table 5: Graphs illustrating the relation between insulin and candle temperatures

a) Water in vessel:500ml; Water in candle:200ml each	
Coolant: NH_4Cl, (53.49g/ 1 mole)	Coolant: $CO(NH_2)_2$, (60.06g/ 1 mole)
	
b) Water in vessel:300ml; Water in candle:200ml each	
Coolant: NH_4Cl, (53.49g/ 1 mole)	Coolant: $CO(NH_2)_2$, (60.06g/ 1 mole)





VI. RESULT

A total of four experiment runs were conducted by changing the coolant in the reaction candles, varying its amount and that of the water in the vessel. It is evident from the first table of graphs that the maximum cooling, i.e., maximum decrease in the temperature of water in vessel along with that of insulin was achieved when the coolant used was 53.49g (1 mole) of ammonium chloride and the water in the vessel was 300ml.

The second table of graphs illustrates the relation between the candle and the insulin temperatures, and the time required for the temperatures to achieve their respective steady values. The graphs of both ammonium chloride and urea when the water taken in the vessel is 300ml, show that the difference between the insulin and the candle temperature is quite small which means that there is an efficient heat transfer taking place from the coolant to the water in the vessel (and subsequently to the insulin). To insure a sustained cooling over long periods of time, the equilibrium of the temperatures should be achieved within the first quarter of the run so the insulin's potency can be maintained. It can be noted that insulin in the aforestated case (300ml of water in vessel) reaches its equilibrium temperature with 30 minutes, thereby reducing the chances of it getting spoilt.

It can be thus inferred that ammonium chloride acts as a better coolant as compared to urea and the cooling in the vessel can be further enhanced by decreasing the amount of water in the vessel, to an amount that insures that the reaction candles are just immersed in order to optimize the heat transfer area. Although experimentally ammonium chloride seems a better coolant than urea, its solubility is less as compared to that of urea ,i.e., more amount of urea can be dissolved in the same volume of water; also urea is highly subsidized and doesn't evolve NH_3 when hydrated. Therefore one needs to consider all the factors and the prototype design while choosing the most optimum coolant.

VII. PROPOSED DESIGN FOR INSULIN STORING THERMOS

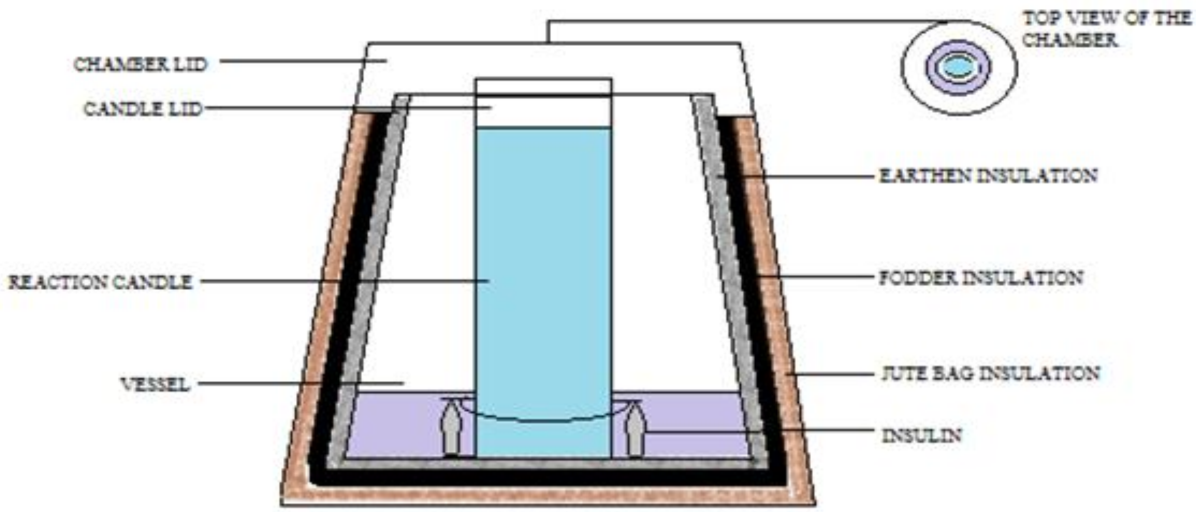


Figure 1: Schematic diagram of the thermos

VIII. Conclusion

Diabetes has emerged as a major healthcare problem in India. In 2007, there were an estimated 40 million persons with diabetes in India according to Diabetes Atlas published by the International Diabetes Federation (IDF), and this number is predicted to rise to almost 70 million people by 2025. By 2030, India along with China and USA will have the largest number of diabetic people. [13] Statistically, the economic burden due to diabetes in India is amongst the highest in the world. According to World Health Organization, in a low-income Indian family with an adult with diabetes, as much as 25% of family income may be devoted to diabetes care. [14] This proportion only worsens as one goes down the economic pyramid. The impact of socio-economic transition occurring in rural India has resulted in an increase of diabetes prevalence from 2.4 per cent to 6.4 per cent of the total population in the last 15 years. It is imperative, therefore to provide economically feasible solutions to the diabetes conundrum, especially for the indigent. The prototype proposed in the paper works on a simple chemical principle and thus the lack of scientific knowledge won't be an impetus, making it an ideal fit for the rural areas. The prototype can not only be used for keeping insulin cool but its use can also be extended to other medications and vaccines by further manipulating the design. The implications of the model in the field of primary health care are immense, whether it is India or third world countries such as the ones in Africa. The model along with being commercially viable on a large scale uses bio degradable materials, as compared to other foam based insulators used in present-day thermos. [15, 16]

In a developing country such as India where 250 million people live in abject poverty, the prerogative of running a universal health care system as envisaged by the Constitution lies not only on the constituent states and territories of India but also on the citizenry.

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