Research Article
Consolidating Tender Coconuts as a Source of Safe Natural Large Volume Parenteral Fluid Under Regulatory Oversight
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Abstract
Purpose: To investigate reported absence of hyperkalemia episodes due to high [K+] and the absence of hypersensitivity reactions due to tracer proteins in tender coconut water following IV infusion. To establish tender coconuts as a prospective natural large volume parenteral ‘dosage unit’. Method: Fluid from nuts identified with ‘Rosette Alba’ sign to be of 5-6 months maturity were evaluated. Important tests performed were the shelf life, direct tapping of the fluid, hemolysis and the molecular mass studies of tracer proteins by SDS PAGE gel electrophoresis. Results: Calculations indicate that [K+] dropped by 1/6th -1/9th in blood following IV infusion of fluid. Proteins are in the low molecular mass range of 10,000 Da, hence below potent antigen range. Conclusion: Drastic dilution of [K+] and the presence of hyperkalemia antidotal ingredients in the fluid and the low molecular mass of the proteins found in low concentration of 0.2 % and IV administration bypassing immunogenic subcutaneous route could be the possible reasons for absence of hyperkalemia and hypersensitivity reactions. The study did not show any dosage parameter that adversely restrains IV infusion potential of tender coconut water.

Key words: Intravenous infusion, coconut water, Cocus nucifera aurantiaca, Rosette Alba, hyperkalemia, antigens, bisphenol A.

Introduction
Only human blood and tender coconut water (TCW) derived naturally from animal and plant sources could be administered intravenously to human beings. This very exclusivity of TCW deserves rigorous researching about its intravenous (IV) infusion potential. It is the liquid endosperm of the fruit, histologically a live liquid tissue as it carries free nuclei undergoing division.(1) In over 70 years of TCW intravenous use, no untoward reactions have been reported.
intravenously to the battle field casualties in remote localities as a stop gap measure. The present study aims for a scientific investigation of the pharmaceutical attributes of TCW as an IV infusion fluid.

In the early days of TCW IV administration, risky manipulations were performed aseptically transferring the fluid into glass infusion bottles. Modern IV administration sets can tap the fluid directly from the nuts at the bedside. The built in bacteria proof air breather and the micro-filter (0.2 micron) attached to the drip chamber removes any stray particles or microbes.

No hyperkalemia symptoms have been ever reported following oral consumption of TCW in volumes of 400-500 ml, equivalent to about 10 g of K⁺. It is postulated that the presence of comparatively high concentrations of Mg²⁺, Ca²⁺ and glucose in TCW mitigate the deleterious effects of high [K⁺] since former three are standard antidotes for hyperkalemia.(2, 3) The present study intends confirming if the high concentrations of these solutes are present in TCW from coconut plants grown in Sri Lanka too.

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Large volume products (LVPs) should be sterile, endotoxin and particle free. These requirements are naturally met by TCW. Industrially fabricated LVPs should meet several other requirements that include identification tests, assays, limit for residual solvents, heavy metals, glucose breakdown products, 5-Hydroxymethylfurfural and the related substances. Further the quality of ‘water for injections’ has to be monitored daily. Evaluation of plastic primary packaging materials involve much more complex mandatory biological tests, largely out of reach of the LVP formulation industry that rely on certificates issued by the plastic manufacturers. Plastics leach out toxic materials such as bisphenol A harmful to human health including the human embryos especially during heat sterilization process.(4) It has estrogenic activity and thus the consequences thereof.

TCW has no such harmful substances nor any need for routine analysis and monitoring of the raw materials or the manufacturing procedures. The industry is greatly relieved of the need for production monitoring and the associated analytical burden.

Complex composition of TCW consists of electrolytes, sugars, sugar alcohols, vitamins, amino acids, fatty acids, organic acids, enzymes and phytohormones adding up to nearly 100 constituents.(1) TCW is held under pressure inside the nuts and any breach in outer covering results in a leakage, a self-evident sign to discard the nut. This natural IV fluid is continued to be generated in inexhaustible quantities in pristine purity. Ironically it is produced in contrast to the modern ‘form, fill and seal’ LVP technology in the reverse order of ‘seal, fill and form’. Strangely 350-600 ml fluid per nut is generated by the coconut palms in the absence of any trace of visible free liquid water in the soil.

The first intravenous infusion was 75 years ago (1942) in Havana by Pradera et al for which only cross references in recent articles are available. In 1954 Ben Eiseman conducted a study for acute and chronic toxicities by administering 250-500 ml of TCW intravenously to dogs at rates of 6 to15 ml a minute. Hypersensitivity studies were conducted with five rabbits for eleven weeks. No evidence of tissue damage in autopsies or hypersensitivity reactions have been recorded. In the same study 300 ml-500 ml
TCW per human subject were administered over a period of 25-180 minutes, no adverse effects were recorded.(5) In 1954 Rajasuriya et al from Colombo General Hospital, Sri Lanka, twenty six patients were treated successfully with intravenous infusion of coconut water. In 1961 in a review article by Goldsmith, the TCW composition table sums up findings of four studies where \([K^+]\) indicated were 53.7, 49, 38.2 and 49 averaging 47.5 mEq/L.(6)

A widely observed ethno-botanical practice in tropical countries is the consumption of about 500 ml TCW in one drinking bout. Hyperkalemia symptoms were never reported despite the fact that potassium is absorbed quickly by oral route and that this route has a pharmacokinetic semblance to the iv infusion in potassium supplementation.(7) Indirectly this shows that TCW IV infusion may not lead to hyperkalemia either.

The healthcare professionals misinterpret the high \([K^+]\) values displayed in TCW composition tables by comparing numerically with those of plasma \([K^+]\) values. They represent two different settings, one in the coconut 47.5 mEq/L in a fluid volume of 0.5 L,(6) The other is in blood 3.5-5 mEq/L in 5.0 L. The fact that TCW gets diluted ten times even if the entire nut volume of 500 ml is IV administered is overlooked. However the large volume high strength \([K^+]\) IV solutions are administered over a number of hours where a surge in \([K^+]\) is unlikely.

Objectives of the study were to dispel the two major concerns about the use of tender coconut water (TCW) for intravenous infusion purpose. These were the high concentration of K’ that might result in toxic hyperkalemia and the presence of uncharacterized peptides that might lead to hypersensitivity reactions. The final objective was to enlist and promote wider acceptance of appropriately labelled tender coconuts by the healthcare professionals and regulatory authorities as a natural LVP infusion ‘dosage unit’.

Methods
The nuts evaluated were from plants in three soil salinity levels, at different distances and elevations including midland and highland away from the seashore. Determinations were done within 48 hours following plucking and fluid drawn immediately before analysis. Experimental details of the procedures are given only for less commonly performed tests.

Applied pharmacognosy and ‘Rosette Alba’
Evaluations were carried out for green or brown fruits of tall variety *Cocus nucifera* L and orange colored king coconuts, *Cocus nucifera aurantiaca*. The younger coconuts have a diffused halo of whitish skin surrounding the perianth. As the fruits grow older it disappears and turns green similar to the rest of the outer skin of the coconuts. The nuts in between these two ages show a sharp whitish lining of about 2-3 mm thick surrounding the perianth proposed here as ‘Rosette Alba’ are the 5-6 month matured nuts (Figure 1).
Figure 1: From left to right: ‘Rosette Alba’ surrounding perianth of a 5-6 months mature coconut. Absence of the same in a fully matured nut. Direct tapping with IV giving set with spike inserted. Note sliced husk at the top with inserted needle.

Physico-chemical tests
The procedures of the British Pharmacopoeia were used wherever they are applicable for routine tests. Instruments used for the determinations are the EUTECH pH6+ double junction refillable for pH, THERMO SCIENTIFIC for the pH measurements and Osmometer Model 3320, ADVANCED INSTRUMENTS, JNT for osmolarity. For the residue on evaporation, specific gravity, pH, conductivity and osmolarity tests, two nuts were harvested from palms grown in each three locations as already described. King coconuts were also analyzed.

Chemical tests
Determination of concentration ranges of Na\(^+\), K\(^+\), Mg\(^{2+}\) and Ca\(^{2+}\) were performed for 6 nuts each from near the seashore and highland. These ions were determined using GBC 932AB+ Atomic Absorption Spectrophotometer iCE 3000, THERMO SCIENTIFIC. Chemical reference substances NaCl, KCl, CaCO\(_3\) and Magnesium dissolved in HCl were used for serial dilutions for the standard curves of these ions. Argentometric method and Vanadomolybdophosphoric acid method respectively were employed in determining anions Cl\(^-\) and PO\(_4^{3-}\) using two nuts each (Table 1).

Test for sterility
Sterility tests were conducted using Mueller Hinton Agar media. Samples were drawn aseptically with a disposable syringe inside a clean bench and spread plates were prepared. Green nut and king coconut from midland were tested using three samples from a single nut each. Sterility tests were performed on day one after plucking and on day four as a part of stability studies.

Test for hemolysis
Mixed approximately 0.5 ml of fresh erythrocytes with 4 ml each of physiological saline, tender coconut water and distilled water in a series of test tubes. No sooner erythrocytes settled to the bottom in distilled water, hemolysis has already set in. For a period of one hour the test tubes were observed for hemolysis. The tests were repeated with tender king coconut water.
Table 1: Tender coconut water test results for green/brown varieties and king coconuts

| Test                        | Location of green/brown trees | King coconut (Midland) |
|-----------------------------|-------------------------------|------------------------|
|                             | Near seashore | Midland | Highland | Midland   |
| Residue on evaporation (mg/100 ml) | 0.9          | 0.95    | 1.25     | 1.35      |
| Specific gravity (30 °C)    | 1.0001        | 1.0001  | 1.0004   | 1.0091    |
| pH (30 °C)                  | 6.24           | 6.17    | 6.12     | 5.11      |
| Conductivity (μS/cm, 30 °C) | -              | 9.8     | -        | 5.47      |
| Osmolarity (mOsmol/Kg)      | 409            | 387     | 352      | 331       |
| Na⁺ mmol/L                  | 1.96           | -       | 2.67     | 0.82-1.1  |
| K⁺ mmol/L                   | 56.44          | -       | 87.82    | 66.68-74.82 |
| Ca²⁺ mmol/L                 | 5.64           | -       | 9.17     | 8.94-9.42 |
| Mg²⁺ mmol/L                 | 8.08           | -       | 15.72    | 5.0-5.65  |
| Cl⁻ mmol/L                  | 58.01          | -       | 62.23    | -         |
| PO₄⁻³ (g/L)                 | 1.25           | -       | 1.29     | -         |
| Sterility on day 4          | -              | Sterile | -        | Sterile   |

Stability studies in assigning shelf life for tender coconuts

The real time stability studies were conducted on the same principle as for regular dosage forms. The time until the initial physico-chemical parameters of the fluid remained unchanged and the fluid also remained sterile is considered as the shelf life. A young coconut bunch was harvested. Two nuts were used every 24 h for duplicate analysis up to eight days. Changes to the concentration of Na⁺, K⁺, and Ca²⁺ were determined with atomic absorption spectrophotometry (Figure 2). The pH was determined using the instrument EUTECH pH6+ double junction refillable for pH, THERMO SCIENTIFIC (Figure 3). Sterility tests were performed for both green and king coconuts on day four as described above under ‘Test for sterility’.

Isolation of tracer protein from TCW

Biuret and Ninhydrin tests confirmed the presence of proteins in TCW. Bradford assay yielded a protein concentration of 0.197%. In the acetone precipitation method, to a volume of 12 ml TCW, 48 ml of 2-8 °C acetone was added and allowed to stand for about 20 minutes at -20 °C until hazy precipitate appeared. The resulting mixture was centrifuged at 4 °C for 10 minutes at 15,000 rpm. The supernatant discarded and pallot was washed again with cold acetone and centrifuged for 5 minutes. The resulting protein was dried in a desiccator and stored at -20 °C.

Determination of molecular mass of peptides

For the molecular mass determination, the SDS PAGE gel electrophoresis procedure of the Department of Chemistry, University of Colombo was followed. According to these procedures preparation of the stacking gel, the separating gel, pH adjustment, degassing, preparations of albumen and TCW protein samples, electrophoresis running conditions (74 mV for 120 minutes), staining and de-staining of the spots were carried out. Finally the spots for reference bovine serum albumen
representing a molecular mass of 60,000 Da and test protein sample were determined (Figure 4). The electrophoresis running time was terminated retaining the solvent front above the lower edge of the gel because no spots were detected in four previous attempts. The TCW peptides appeared to have run off the lower edge of the gel due to possible small molecular mass.

Technique of direct tapping of the nut
The tapping technique needs much practice since the nuts are rigid resisting fluid flow unlike the flexible plastic containers. The stalk end of aseptically treated king coconuts were sliced 10-20 mm away from the circumference of the perianth in a circular cut ensuring that there is sufficient soft ‘husk meat’ between the exposed surface and the fluid cavity inside the nut. This facilitates firm hold of the spike of the IV giving set and to prevent leakage of fluid (Figure 1). A sterile stainless steel sharp knife must be used to cut, mindful that minimum particles are generated. Avoid saw like motion to minimize particle generation and hammer like motion that impact the fruit leading to formation of fine cracks.

The IV administration sets were from ROMSONS JUNIORS INDIA, RMS VENTED INFUSION SET for gravity feed with Y injection site and 21G X 1.5 inch needle. Four tapping schemes were attempted by manipulating as required, the air vent in the spike, flow control, creating vacuum by aspirating air at the injection port with a disposable syringe and inserting a second needle at the opposite end of the nut to that of the stalk end. The spike was inserted in to cut surface in one straight gentle push up to the base of spike. All sideways or rotating motions should be kept to a minimum so that the spike will be gripped firmly.

In all cases pieces of soft husk ‘meat’ was found in spike openings meant for air and fluid flow. In the first nut fine fiber particles were observed in the drip chamber probably because a hacksaw was used to cut the nut.

Model calculations of resulting serum [K+] when 300 ml TCW is IV administered
According to British National Formulary 2011, there are three proprietary IV preparations SYNTHAMIN 9, SYNTHAMIN 14 and SYNTHAMIN 17 containing 60 mmol/L (or mEq/L) of K⁺ in 500 ml packs manufactured by BAXTER, which are very similar to the volume and the [K⁺] in TCW.(8) This shows that there is scope for the TCW also to be accepted for the same therapeutic purpose.

Assuming that K⁺ remains within the circulatory system and that no K⁺ ions are excreted during the period under consideration, calculations were based on a [K⁺] strength of 60 mEq/L. The At. Wt. of K 39 is also the equivalent weight. The mEq of K = 39 /1000 = 0.039 g. Weight of 60 mEq/L of K = 60 x 0.039 g = 2.340 g/L of TCW. The amount of K in 0.3 L = 2.340 X 0.3 = 0.702 g.

Consider the average [K⁺] in human serum is 4.25 mEq/L (range 3.5 – 5 mEq/L). Therefore weight of K⁺ in human serum = 4.25 X 0.039 g/L = 0.165 g/L. Taking 2.5 L as the volume of serum, weight of K⁺ in serum will be 0.165 X 2.5 g or 0.413 g.

Assuming that 300 ml TCW with 0.702 g K⁺ is iv infused and no excretion or no intracellular partition takes place the
resulting serum $[K^+]$ will be $0.702 \text{ g} + 0.413 \text{ g}/\text{total volume} = 1.115 \text{ g} / (2.5 \text{ L}+0.3 \text{ L}) = 0.4 \text{ g}/\text{L}$. Final serum $[K^+]$ will be $400/39 \text{ mEq}/\text{L}$ or $10.2 \text{ mEq}/\text{L}$.

Now, assuming that half the $K^+$ in IV infused TCW partitions into cells including erythrocytes, the remaining serum $K^+$ will be $0.702 \text{ g}/2 = 0.351 \text{ g}$. Therefore resulting total amount of potassium following IV infusion in $2.5 \text{ L}$ serum + $0.3 \text{ L}$ TCW = $0.413 + 0.351 \text{ g} = 0.764 \text{ g}$ or $764 \text{ mg}/2.8 \text{ L}$. Amount per liter = $764/2.8 = 273 \text{ mg}$ or $273/39 \text{ mEq}/\text{L} = 7 \text{ mEq}/\text{L}$. The $[K^+]$ therefore settles down to 6 - 9 times fraction of the strength in TCW following IV administration.

**Results and Discussion**

The identification of 5-6 months maturity nuts based on the 2-3 mm wide ‘Rosette Alba’ lining is a useful finding (Figure 1). The best method of determining maturity time is to tag the inflorescence as the sheath opens up exposing the flowers in which case one month has to be added for pollination time in determining age of coconuts.

The following could be suggested for the reliable and effective management of coconut palms dedicated for the infusion purpose. Harvesting of the tender coconuts for infusion purpose must be according to all applicable good manufacturing practices (GMP) under the supervision of a trained person. A distinction must be made between harvesting for commercial and medicinal uses. The coconut bunch should be tied, lowered on to a clean receptacle avoiding undue jerk, mechanical shock or injury to the nuts. The selected defect free nuts should be cleaned and stored as per GMP requirements. Similar to regular iv solutions the nuts must be labeled in line with requirements under regulations, ‘Tender Coconut for Intravenous Infusion’ indicating the location, the identity of the tree, date and time of plucking, date and time of expiry together with the signature of the responsible officer. The label should indicate concentration ranges of the constituents of TCW that matter, $Na^+$, $K^+$, $Ca^{2+}$, $Mg^{2+}$, $PO_4^{3-}$, sugar and the osmolarity according to available data. It is preferred that an international body of experts publish a data sheet for the purpose. Appropriate batch records of all harvesting events must be maintained. The nuts should be now treated as a ‘dosage form’ and liable for drug regulatory inspection.

Most physico-chemical test results for king coconut and TCW are similar to what had been already published. The osmolarity range detected 331 – 409 mOsm/kg is higher than the normal plasma values, 280 – 300 mOsm/kg. The lowest value 331 mOsm/kg is for king coconuts (Table 1). However this range appear to be compatible as no hemolysis was observed in 1 h which was also the case for control samples of physiological saline. Further the osmolarity values would tend to shift rapidly towards normal range since even a volume of 500 ml TCW is diluted ten times following IV infusion. There are many IV infusions such as KCl 0.15%, NaCl 0.9% and Glucose 5% Infusion with an osmolarity of 625 mOsm/L. Hemolysis was observed for distilled water. Nuts from three saline soils yielded similar values except high osmolarity for sample near seashore. Most parameters of king coconut water are somewhat lower than the regular varieties. It could possibly be freely interchanged with the regular varieties for IV infusion. In a single Coulter Counter determination for a 5-6 months mature nut
the fluid was found to be particulate matter free. Gelatinous liquid precipitates (coacervates) can be sometimes observed when TCW is collected in stainless steel vessels.

The \([K^+]\) detected 56.44–87.824 mmol/L in the present study is higher than in other studies. (5, 6) It is drastically higher than 6.0 mmol/L for mild and 7.0 mmol/L for severe forms of hyperkalemia. The high \emph{prima facie} \([K^+]\) values displayed in TCW composition tables were found to settle at much lower intravascular values following IV infusion. According to calculations the plasma values were 10.2 mEq/L and when 50% of \(K^+\) from TCW is assumed partitioned intracellular it is 7.0 mEq/L. Considering the high proportion of 98: 2 intracellular to extracellular partitioning of \(K^+\), it is more likely that the \emph{in vivo} result could be lower than 7.0 mEq/L. These unfavorable results were arrived without accounting for \(K^+\) excretion, neutralization of hyperkalemia effects due to presence of high concentrations of Ca\(^{2+}\), Mg\(^{2+}\) and glucose in TCW and assuming that 300 ml TCW was infused all at once.

Standard treatment for hyperkalemia among other measures involves intravenous administration of calcium gluconate and glucose. (2) Magnesium sulfate is also used to counter cardiac arrhythmias particularly in relation to hypokalemia. (9, 3) These indications show that the high concentrations of Ca\(^{2+}\), Mg\(^{2+}\) and glucose present in TCW may mitigate the possible effects of hyperkalemia following TCW infusion.

Merck Manual normal serum (S) values are compared with values of TCW under present study for the two ions Mg\(^{2+}\) and Ca\(^{2+}\) (Table 1). The values in mmols/L are, \([\text{Mg}^{2+}]\): 0.6-0.99 (S) against 5.0-15.7 (TCW); \([\text{Ca}^{2+}]\): 2.2-2.6 (S) against 5.6-9.4 (TCW). Considering normal blood glucose level 100 mg/100 ml, and 1200 mg/100 ml for TCW, the proportion is 1:12. (10) Hence TCW has higher concentrations of 5, 3 and 12 times of these substances respectively compared to serum values. Therefore TCW tends to raise their blood levels and possibly are therapeutically effective in mitigating hyperkalemia. It is difficult to quantify dose requirements for TCW which is also the case for commercial LVPs for IV infusion. Many depend on the type and condition of the patient. The electrolyte, electrocardiographic and other necessary tests should be carried out for TCW similar to regular LVPs.

The calculation did not consider the relevance of maximum infusion rate of 300 ml administered over a period of 2.5 h as in the case of potassium chloride and glucose intravenous infusion having a \([K^+]\) of 40 mEq/L. (11) During this period excretion of \(K^+\) can take place resulting in lower plasma concentration. The swift adjustment of high \([K^+]\) to normal extracellular range of 3.5–5.0 mEq/L by physiological mechanisms could be another factor in the mitigation process.

In shelf life determination the graphs for \([Na^+]\), \([K^+]\), \([Ca^{2+}]\) and \(pH\) against time, characteristic deflections were observed on the 7\(^{th}\) day (Figure 2, 3). These changes represent signs of deterioration of the integrity of the nut. It is safe to assign an expiry of 5 days (120 hours) from the time of plucking. Any changes due to TCW pH values will be dealt with by physiological buffer systems of blood. Absence of hemolysis and particulate matter in TCW have cleared two important requirements for any IV infusion fluid. Tests on days one and four after plucking were found to be sterile.
Autoclaving TCW should be avoided since proteins coagulate resulting in turbidity.(5)

In the molecular mapping of the spots, with respect to bovine serum albumin (60,000 Da) the spots for TCW protein is at the solvent front indicating a molecular mass of 10,000 Da since with reference to ‘rainbow reagent’ the value of the spot closest to solvent front is 6000 Da (Figure 4). For a protein to be actively immunogenic the molecular mass has to be between 14,000–60,000.(12,13) Further the soluble proteins as against particulate proteins, IV administration bypassing immunogenic subcutaneous route and that low concentrations of the protein (0.2%) make these TCW proteins antigenically ineffective.(13)

Two other rare varieties of king coconuts, dull pale yellow colored (Sinhala; Gon Thembili) and outer orange colored but when cut the exposed surface of the tender husk with a pink hue (Sinhala; Ran Thembili) grow in Sri Lanka. Another dwarf green coconut (Murusi variety) can also be found. These varieties need to be investigated in anticipation of more favorable results with respect to [K+] and tracer proteins.
Positive findings under this study include that i) it is inappropriate to numerically compare TCW composition table values of $[\text{K}^+]$ with those of serum values. ii) the presence of hyperkalemia antidotes $\text{Ca}^{2+}$, $\text{Mg}^{2+}$ and glucose in relatively high concentrations in TCW appear to neutralize the effects of high $[\text{K}^+]$, iii) the low molecular mass peptides in very low concentrations are likely to be non-antigenic, iv) toxic substances generated by plastic containers are absent, v) needs in production and analytical inputs connected to TCW is nominal and vi) assigning a shelf life of 120 hours to tender coconuts. The sterility, absence of particulate matter and non-hemolytic properties of the fluid present in volumes of 300–600 ml per nut firmly establishes it as a prospective large volume parenteral. The use of ‘Rosette Alba’ as a morphological identity criterion for 5–6 months mature nuts is another useful finding. On direct tapping of nuts, insertion of a second needle appear to be the best method (Figure 1). The composition indicates that TCW belongs to the category of a potassium and fluid supplementing LVP. TCW may be useful as an alternative to sterile water for injections in dilution and reconstitution of small volume parenterals.

The draw backs of TCW as an iv fluid are that i) the fluid inside the nuts is not visible for inspection, ii) possibility of generating particles on the cut surface of the nut, iii) lodging of particles in the pores of the spike meant for the fluid and air transfer, iv) the excessive $[\text{K}^+]$ that tend to resist its use despite all evidence for absence of hyperkalemia episodes, v) wide range of concentrations of the constituents of the fluid and vi) short safe shelf life of 120 hours after plucking the nuts.

**Conclusion**

Two of the main impediments in the use of TCW for IV infusion purpose among healthcare personnel have been effectively cleared. The study revealed that the apprehensions regarding the very high $[\text{K}^+]$ values displayed in TCW composition tables are ill-founded since the ion gets diluted almost ten times following infusion. The hyperkalemia neutralizing agents $\text{Ca}^{2+}$. $\text{Mg}^{2+}$ and glucose found in comparatively high concentrations in TCW possibly antidote the toxic effects of $[\text{K}^+]$ as these are the standard antidotes in the treatment of hyperkalemia. With regard to hypersensitivity reactions, the protein or peptide traces that amounts to a very low concentration of 0.2% in TCW were found to be in the low molecular weight range. The value around 10,000 Da is possibly insufficient to qualify these as antigens. This means that the hypersensitivity reactions are unlikely to occur with TCW. Other significant findings of the study are the identification of ‘Rosette Alba’, determination of shelf life for the nuts, the technique for direct tapping of the fluid from the nuts and the absence of hemolysis.

Normal values for TCW constituents need to be established by an international agency in the same lines as normal plasma values. A formal Phase I clinical trial need to be undertaken by a team of experts on LVP infusion therapy. Drawing up a comprehensive product information leaflet for tender coconuts as a LVP IV infusion dosage form acceptable to official regulatory bodies will be the final hurdle in the consolidation process.
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