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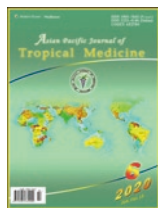
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## Perspective

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## Immunized camels and COVID–19

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The World Health Organization (WHO) declared coronavirus disease-2019 (COVID-19), a global pandemic on 11th March 2020, as its causative virus "severe acute respiratory syndrome coronavirus-2" (SARS-CoV-2) spreads rapidly out of control across the world[1]. A few months ago, the virus has spread all over the world claiming the lives of thousands of people, and hundreds of thousands being infected on daily bases and the numbers are on the increase[1,2]. This pandemic puts enormous pressure on health services across the globe, especially as it coincides with the seasonal flu. Therefore, all efforts to control this new pandemic are needed.

The WHO recommended different prevention steps and many governments have already implemented them with the hope to reduce the spread of infection through social, behavioural and quarantine methods. However, the virus clearly overwhelmed all these current efforts as new number of infections and mortalities are on the increase[1].

The question of great importance: "would there be a vaccine to prevent SARS-CoV-2 infection and when would it be available?" The answer to this critical question is most probably "yes", but would the expected vaccine be available soon enough to help those in critical need and save lives, and would it be affordable to all in need, especially in the underdeveloped countries? The current crisis led many countries to declare national emergencies including the United States of America. We are now in a race with time searching for a vaccine to prevent SARS-CoV-2 infection and to find a cure for COVID-19. Therefore, an urgent need exists for a simple and affordable strategy to help those infected, to prevent further infections, to reduce the heavy burden on health services, and to stop this new pandemic.

Camels are well-known hosts to harbour different strains of the coronaviruses[3] and able to produce good immune responses to these viruses. Although camels may be a source of human infection with the Middle East respiratory syndrome coronavirus (MERS-CoV)[3], camels can still be used as important vehicles for generating strong immune responses against different strains of the coronaviruses. Hence, infecting lactating female camels

with an inactivated form of the current coronavirus strain (SARS-CoV-2) will lead to a significant immune response against the virus components with the generation of specialized small camel IgG antibodies both in camel' serum and milk[4].

These nano-antibodies have the ability to penetrate into tissues[5], neutralise viruses outside and inside infected cells[6], stable at high temperatures of up to 80 °C[7], resist stomach enzymes digestion such as pepsin and trypsin[7] and therefore able to gain access into the blood stream as intact antibody molecules[6,7]. Moreover, camelid IgG is also less immunogenic than most mammalian IgG[8]. This is due to the fact that intravenous administration of camelid anti-venom is less likely to induce serum sickness and anaphylactic adverse reactions associated with equine and ovine anti-venom treatment[8]. This is similar to the promising and successful strategy we have invented and implemented in the phase I clinical trial for the treatment of HIV patients, with a patent granted by the US Patent Office in 2016[6].

Studies on camelid immunoglobulins provide a compelling rationale for the development of a strategy of an antibody-based approach for the neutralization of SARS-CoV-2. This novel strategy of using the unique camel's immune system, as illustrated in Sultan Qaboos University (SQU) patent[6], is based on the fact that approximately half of camelid immunoglobulins lack light chains and the 15 kDa antigen-binding domain of the heavy chain antibody (V<sub>H</sub>H, obtained by protease cleavage) is significantly smaller than papain-cleaved Fab (60 kDa) fragments of conventional human

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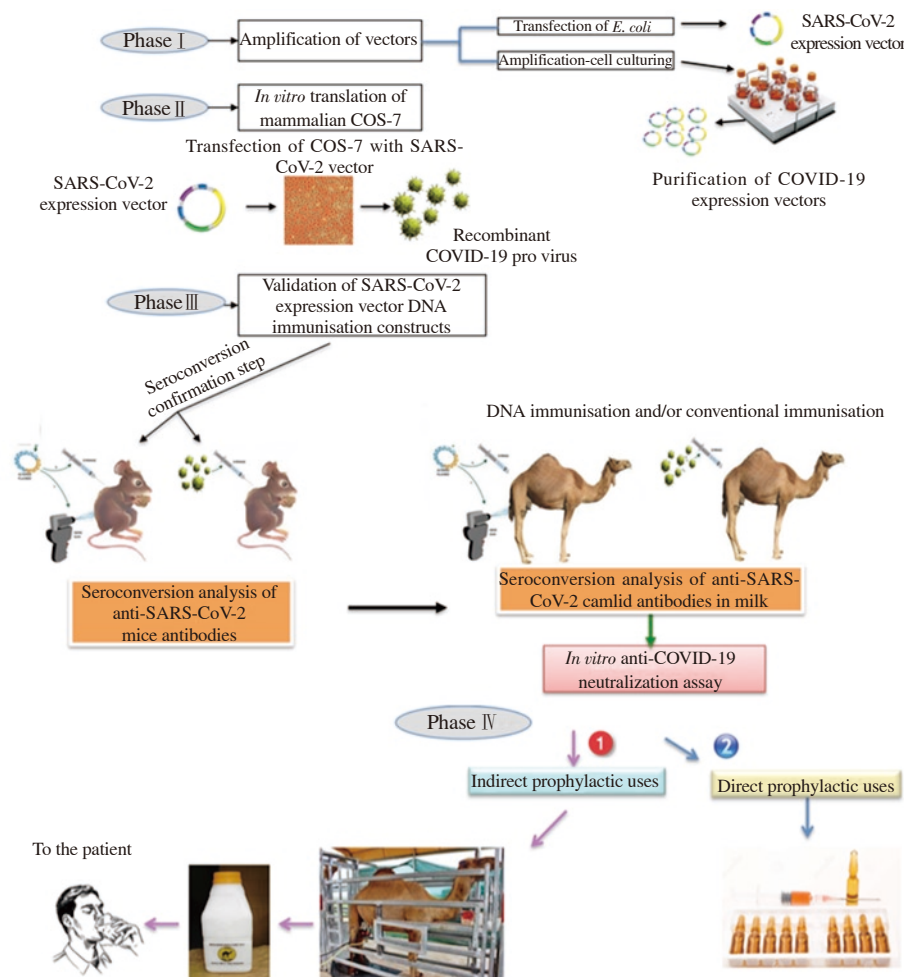
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IgG[4]. Moreover, antigens-specific recombinant V<sub>H</sub>H, intravenously injected into tumor-bearing transgenic mice, were shown to penetrate and bind the deep-tissue located target antigens within two hours, and were retained in tissues for more than eight hours after administration[5]. This rapid tissue-ingress of intravenously injected V<sub>H</sub>H has obvious potential for the treatment of viral infections.

Studies have shown that camel's immune system is a much stronger immune system than human, and its milk is adequate and effective among the other ruminant milk against microorganisms including *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhimurium*, and rotaviruses[9]. Camel milk has its unique nutritional composition and is rich in minerals, vitamins, low sugar and cholesterol and has a significant antioxidant effect[9,10]. In addition to the secretory IgA and IgM, as well as the small IgG antibodies, camel milk also possesses numerous non-antibody components such as lysozyme, lactoperoxidase and lactoferrin among others, with their scientifically proven effective antimicrobial activity, especially antiviral activity[9,10].

Currently, there is no cure for COVID-19 and attempts to produce a preventive vaccine against the virus are on the way. Therefore, we predict that using camelid to generate antibodies including the “V<sub>H</sub>H” will potentially and selectively inhibit and neutralise SARS-CoV-2. This strategy involved efficacy *in vitro* evaluation of the generated anti SARS-CoV-2 camel antibodies, using standard scientific methods, and *in vivo* clinical trials study phase as outlined in Figure 1.

The neutralizing antibodies in the milk of immunised camels will give passive immunity to those with COVID-19 as a treatment or even can be given as a mean of prophylaxis to prevent those at risk of SARS-CoV-2 infection. Milk obtained from the immunized camels, after sterilisation, can be given to the patient infected with SARS-CoV-2, three times a day (300 mL) for three to five days (depending on the patient clinical complications) for the complete neutralisation of the virus in the same manner to that of the SQU-patent[6]. People at risk of infection, such as elderly people, patients with other serious medical complications and healthcare workers could be the initial target for such treatment. In addition to this new



**Figure 1.** An outline schematic diagram showing the main phases of the strategy. The strategy consists of three main phases (I, II & III) and a clinical trial phase (IV). The three phases are: vector amplification; *in vitro*-translation of mammalian COS-7; and validation of the SARS-CoV-2 expression vector for DNA immunisation. The three phases involve standard scientific methods, both *in vitro* and *in vivo*, for raising antisera in animals and standard tests to confirm the production of the antisera. Anti SARS-CoV-2 camel antibodies efficacy must be confirmed *in vitro* as well as its safety prior it's used in the clinical trials. Ethical clearance must be obtained from the relevant authorised bodies prior to conducting this proposed strategy.

SARS-CoV-2 proposed treatment strategy, patients may also get the benefit of taking other immuno-stimulants, under medical care to enhance their own natural immunity against COVID-19.

Moreover, the strategy involves the isolation and purification of the raised antisera against SARS-CoV-2 and the utilization of these unique neutralizing antibodies, after carefully disinfecting any residues of viruses and other microbes by standard sterilisation methods. Once its efficacy and safety is confirmed, the purified antisera against SARS-CoV-2 can be transfused directly to the blood stream of the infected patient. This is in the same manner where current anti-snake venoms are generated and used.

Camels stock is available all over the world and can be used as mobile live factories to synthesise and produce these amazing neutralizing antibodies to treat COVID-19. We strongly believe that, camel milk with camel SARS-CoV-2-antisera, can be made safe and would be available and affordable worldwide to all in need. The method to generate these safe-neutralizing antibodies can be developed and used under careful control of health authorities and according to international standards, similar to those being currently used for the anti-snake venoms production. Such a novel treatment/prevention proposed strategy must be first tested both *in vitro* and *in vivo* and then confirmed in clinical trials, as per international standards and ethics before being made available to all in need. We believe, if such a strategy is known to the international scientific community, the time needed to test and confirm its efficacy will be very much shortened.

As an initiative to help humanity at this very critical time, we invite and encourage all researchers, research laboratories and research institutions all over the world to test and confirm the proposed strategy, of using lactating female camels as live factories to synthesise the desired antibodies, as a mean not only to prevent SARS-CoV-2 infection and to help in stopping COVID-19 pandemic, but also to confirm the use of this strategy against other viral and microbial infections.

### Conflict of interest statement

The authors declare that there is no conflict of interest.

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### Authors' contributions

S.S.H. and A.A.A. equally contributed to the conception, design of the work, data analysis and interpretation, drafting and critical revision of the manuscript and final approval of the version to be published. S.S.H. contributed significantly to data collection and experimental field work.

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