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Combined Covid 19 vaccine and DAILY oral Intralipid or Soybean oil (main component of Intralipid) for the eradication of the Corona Pandemic

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"The doctor of the future will no longer treat the human frame with drugs, but rather will cure and prevent disease with nutrition." Thomas Edison

Abstract
Recently, differences in mortality rates of COVID-19 in different geographic areas have become an important subject of research because these different mortality rates appear to be associated with mutations that appeared in SARS-CoV-2.
Lipids have key functions in signaling pathways, energy storage, and the structural integrity of cell membranes. They also function in host-pathogen interactions and immunomodulation since they act in first-line recognition and host cell signaling during pathogen docking, invasion, and intracellular trafficking .Lipid metabolism and cellular lipids are greatly affected by virus infections by inducing major lipid modifications within host cells through the production of convoluted membranes and double membrane vesicles (DMVs). Virus-induced production of membrane networks and organelles is a common occurrence among all positive sense RNA viruses.
The idea that intravenous lipid emulsion could be used to affect the pharmacokinetics of a drug in circulation was first introduced fifty years ago.
Intralipid® 20% (A 20% I.V. Fat Emulsion) Pharmacy Bulk Package is a sterile, non-pyrogenic fat emulsion intended as a source of calories and essential fatty acids for use in a pharmacy ad- mixture program. It is made up of 20% Soybean Oil, 1.2% Egg Yolk Phospholipids, 2.25% Glycerin, and Water for Injection. In addition, sodium hydroxide has been added to adjust the pH so that the final product pH is 8. pH range is 6 to 8.9.
It is the first time that Soybean Oil is suggested as a daily oral treatment which is Combined to the regular Covid 19 vaccine for the eradication of the Corona Pandemic. It is the first time that a daily soybean oil is given to supplement daily the current vaccines which are given periodically. The soybean oil which is the main component of the Intralipid has already a long history of rescue in many medical problems.

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I. Emerging Mutation in SARS-CoV-2 Spike

Recently, differences in mortality rates of COVID-19 in different geographic areas have become an important subject of research because these different mortality rates appear to be associated with mutations that appeared in SARS-CoV-2. The part of the viral body called the spike protein plays a critical role in the viral attachment and entry of the virus into the host cell. Accordingly, we hypothesized that mutations in this area will affect viral infectivity.

A total of 193 sequences of spike SARS-CoV-2 were randomly retrieved from five different geographic areas and collection dates (from December 2019 until July 2020). Multiple sequence alignment for mutation and phylogenetic analyses was conducted using Bioedit, UniProt, and MEGA X. We found 169 total mutations with 37 different mutations across the included samples. The

D614G is the first and most frequently established mutation in different regions including Europe, Asia, America, Africa and Australia with the number of mutations of 49, 33, 17, 16 and 4, respectively. Furthermore, we also found mutations in several important domains in this virus including NTD and CTR/RBD of S1 subunit and at S2 subunit area, namely the peptide fusion (FP), and both heptad repetition (HR1 and 2) domains that suggested this could influence virus binding and membrane-host cell membrane fusion.

In summary, we concluded that mutation had generated diversity of spike SARS-CoV-2 sequences worldwide and is still growing. This analysis may provide important evidence that should be considered in vaccine development in different geographic areas (1).

Can Intralipid (lipid emulsion) INACTIVATE the Coronavirus?

On February 14, 2020 Joseph Eldor published on Linkedin the following post:

"The LAST Protocol already SAVED the lives of many patients worldwide including in other toxicities and diseases.

It was already suggested for many other diseases.

Be aware that most of the medical innovations were based on SERENDIPITY.

Can Intralipid (lipid emulsion) INACTIVATE the Coronavirus?

Someone in CHINA MUST to test it !" (2).

"Lipids have key functions in signaling pathways, energy storage, and the structural integrity of cell membranes. They also function in host-pathogen interactions and immunomodulation since they act in first-line recognition and host cell signaling during pathogen docking, invasion, and intracellular trafficking .Lipid metabolism and cellular lipids are greatly affected by virus infections by inducing major lipid modifications within host cells through the production of convoluted membranes and double membrane vesicles (DMVs). Virus-induced production of membrane networks and organelles is a common occurrence among all positive sense RNA viruses. The roles of these virus-induced DMVs are not fully understood; however, evidence suggests some viruses may use them for replication, to conceal viral RNA from host antiviral response, or they may have roles in autophagy as autophagosomes." (3).

The first Intralipid rescue of COVID 19 by INTRALIPID was done in IRAN

"Abstract Objectives:

Covid-19 lung involvement is accompanied by morbidity and mortality. There is no efficient drug for treatment of progressive lethal pulmonary invasion of Covid19. Based on unsuccessful results of antiviral medications in the treatment of pulmonary dysfunction, different pathophysiology of pulmonary infiltration should be in mind. Based on hypothesis of progressive blockade of cardiopulmonary system by viral aggregation we are proposing Intralipid infusion for strenuous cleansing the cardiopulmonary system of Covid19 colonization. This article is aimed to report a case of Covid-19 with severe pulmonary involvement. Pulmonary dysfunction subsided obviously after 48 hours of initiation of Intralipid infusion.

Results: In our case, pulmonary dysfunction subsided obviously after 48 hours of initiation of intralipid infusion and obvious improved O2 saturation was observed. We believe that the probable cause of death is disseminated cardiopulmonary involvement by viral load and viral intoxication. Based on this attitude Intralipid is recommended for rescue therapy in Covid-19 pulmonary involvement.

Keywords: Covid-19; Intralipid Rescue Therapy; Pulmonary Dysfunction; Packed Cell; Toxification" .

" Case Presentation:

A 65-year-old male patient, with the history of diabetes and hypertension was presented to the hospital by mild dyspnea on march 14. The initial Symptoms started by fever on march 10, 2020. Diarrhea started on march 11 and lasted for two days and then ceased. The patient was admitted to the hospital on march 14. No medical therapy was received by patient. On the day 5 after hospitalization, sudden drop in blood pressure (70/40 mmHg) and Spo2 (less than 70%) resulted in deterioration of consciousness and urgent tracheal intubation. Mechanical ventilation was stablished and infusion of dopamine was administered. The laboratory tests showed severe changes. WBC: 7300, RBC: 4.05, HG: 11.2, neutrophil: 90%, lymphocyte: 5%, Albumin 2.5gr/dl. Anaemia and Hypoalbuminemia were progressive. Chest CT detected massive pulmonary involvement with grave inflammation (Figure 1). After tracheal intubation and establishment of mechanical ventilation, inotropic dose of dopamine continued for two days. on the day 3 besides conservative cardiovascular treatment, aggressive rescue therapy was proposed as bellow; Infusion of Intralipid 10%, 500 mL for 2 days and infusion of packed cell 1 unit for two days, in order to substitute destroyed RBCs to achieve enough oxygen carrying capacity. Progressive improvement of vital signs and GCS was observed after administration of intralipid and packed cell. Prominent recovery was detected in lung control CT (Figure 2) after aggressive treatment with intralipid and packed cell. After one week, patient was extubated and 48 hours later he was transferred to the ward." (4).

Intralipid in the Target Treatment of Lipid Peroxidation Disorder

"In the current proposal, we used the intralipid in standard therapy against COVID / 19 as an energy carrier for parenteral nutrition in critically ill patients. In patients receiving intralipid, there was an accelerated recovery of the lungs, a decrease in markers of endogenous intoxication (EI), tissue hypoxia and an improvement in general condition. In the absence of Intralipid in the intensive care unit, there was a slow recovery of the lungs and a more prolonged improvement in the general condition with the preservation of EI markers (cytolytic enzymes, C-reactive protein, platelets) and tissue hypoxia (pCO2 AV> 6 mm Hg).

Collectively, Intralipid has been seen in the targeted LPO treatment plan for oxidative and nitro-galogenic stress in SARS-Cov2 / COVID / 19 patients.

Scientists Eldor J., Javid M.J., Zebardast J. has been published [1-8] the successful use of intralipid in postoperative cognitive impairments, the antitoxic effect of local anesthetics during neuraxial anesthesia, and also as an antidote to the toxic manifestations of calcium blockers, and since 2020, the anticovid / 19 effect.Coronavirus enters intracellularly thanks to both the molecule the protein Cluster of Differentiation (CD147) [also called extracellular matrix metalloproteinase inducers (EMMPRIN), or basigin (BSG), and belong to the immunoglobulin superfamily] and the AngiotensinConverting Enzyme 2 (ACE2) receptors due to immunocompromising (IC) mechanisms".(5).

Intravenous lipid emulsion

The idea that intravenous lipid emulsion could be used to affect the pharmacokinetics of a drug in circulation was first introduced fifty years ago. It was shown that rats infused lipid emulsion after an injection of the barbiturate thiopental emerged more rapidly from anaesthesia than rats infused the same volume of fat-free solution (Russell & Westfall 1962) (6). Other early studies were published on the effect of lipid emulsion on chlorpromazine availability in rabbits (Krieglstein et al. 1974) (7), and the effect of lipid emulsion on the elimination of phenytoin (Straathof et al. 1984) (8). Although the studies show some effect of lipid emulsion, this did not kindle more widespread interest in the subject. The serendipitous discovery of the apparently shielding effect of a large intravenous dose of lipid emulsion against bupivacaine toxicity in rats triggered renewed interest in the field (Weinberg et al. 1998) (9). Additional experimental animal and isolated heart studies were performed (Weinberg 2002; Cave & Harvey 2009a) (10-12), and although efficacy and safety had not been established by clinical trials, clinicians soon applied lipid therapy to seemingly hopeless cases of severe intoxication (Rosenblatt et al. 2006) (13).

Intravenous lipid emulsion therapy for severe intoxication is a relatively young field. Although a few early studies on the pharmacokinetic effects of intravenous lipid emulsion exist (Russell & Westfall 1962; Krieglstein et al. 1974; Straathof et al. 1984; Minton et al. 1987) (6-8;13) , its use as a treatment for severe intoxication was proposed as late as 1998 (Weinberg et al. 1998) (9). Since this proposal, no randomized controlled human trials have been published. Thus, the evidence supporting this use of lipid emulsion consists only of animal studies and human case reports of varying quality (Cave et al. 2011) (14).

The basis of Intralipid

Intralipid® 20% (A 20% I.V. Fat Emulsion) Pharmacy Bulk Package is a sterile, non-pyrogenic fat emulsion intended as a source of calories and essential fatty acids for use in a pharmacy ad- mixture program. It is made up of 20% Soybean Oil, 1.2% Egg Yolk Phospholipids, 2.25% Glycerin, and Water for Injection. In addition, sodium hydroxide has been added to adjust the pH so that the final product pH is 8. pH range is 6 to 8.9.

The soybean oil is a refined natural product consisting of a mixture of neutral triglycerides of predominantly unsaturated fatty acids.

The major component fatty acids are linoleic acid (44-62%), oleic acid (19-30%), palmitic acid (7-14%), a-linolenic acid (4-11%) and stearic acid (1.4-5.5%).

It means that the various effects of Intralipid are based 63% to 92% on linoleic acid and oleic acid.

Linoleic acid belongs to one of the two families of essential fatty acids, which means that the human body cannot synthesize it from other food components.

Linoleic acid

Linoleic acid ($C_{18}H_{32}O_2$).

A carboxylic acid, is a polyunsaturated omega-6 fatty acid, an 18-carbon chain with two double bonds in cisconfiguration. A shorthand notation like “18:2 (n-6)” or “18:2 *cis*-9,12” may be used in literature. It typically occurs in nature as a triglyceride ester; free fatty acids are typically low in foods.

Linoleic acid belongs to one of the two families of essential fatty acids, which means that the human body cannot synthesize it from other food components.

The word “linoleic” derived from the Greek word *linon* (flax). *Oleic* means “of, relating to, or derived from oil of olive” or “of or relating to oleic acid“ because saturating the omega-6 double bond produces oleic acid.

Lipid Emulsion - Mitochondrial Sink Effect

Papadopoulou A et al. (15) hypothesized that by substituting a dye surrogate in place of local anesthetic, they could visually demonstrate dye sequestration by lipid emulsion that would be dependent on both dye lipophilicity and the amount of lipid emulsion used.

They selected 2 lipophilic dyes, acid blue 25 and Victoria blue, with log P values comparable to lidocaine and bupivacaine, respectively. Each dye solution was mixed with combinations of lipid emulsion and water to emulate "lipid rescue" treatment at dye concentrations equivalent to fatal, cardiotoxic, and neurotoxic local anesthetic plasma concentrations. The lipid emulsion volumes added to each dye solution emulated equivalent intravenous doses of 100, 500, and 900 mL of 20% Intralipid in a 75-kg adult. After mixing, the samples were separated into a lipid-rich supernatant and a lipid-poor subnatant by heparin flocculation. The subnatants were isolated, and their colors compared against a graduated dye concentration scale.

Lipid emulsion addition resulted in significant dye acquisition by the lipid compartment accompanied by a reduction in the color intensity of the aqueous phase that could be readily observed. The greatest amount of sequestration occurred with the dye possessing the higher log P value and the greatest amount of lipid emulsion.

This study provides a visual demonstration of the lipid sink effect. It supports the theory that lipid emulsion may reduce the amount of free drug present in plasma from concentrations associated with an invariably fatal outcome to those that are potentially survivable.

Local anesthetic (LA) intoxication with cardiovascular arrest is a potential fatal complication of regional anesthesia. Lipid resuscitation has been recommended for the treatment of LA-induced cardiac arrest. Aim of the study (16) was to compare four different rescue regimens using epinephrine and/or lipid emulsion and vasopressin to treat cardiac arrest caused by bupivacaine intoxication.

Twenty-eight piglets were randomized into four groups (4 × 7), anesthetized with sevoflurane, intubated, and ventilated. Bupivacaine was infused with a syringe driver via central venous catheter at a rate of 1 mg·kg−1·min−1 until circulatory arrest. Bupivacaine infusion and sevoflurane were then stopped, chest compression was started, and the pigs were ventilated with 100% oxygen. After 1 min, epinephrine 10 μg·kg−1 (group 1), Intralipid (®) 20% 4 ml·kg−1 (group 2), epinephrine 10 μg·kg−1 + Intralipid (®) 4 ml·kg−1 (group 3) or 2 IU vasopressin + Intralipid (®) 4 ml·kg−1 (group 4) were administered. Secondary epinephrine doses were given after 5 min if required.

Survival was 71%, 29%, 86%, and 57% in groups 1, 2, 3, and 4. Return of spontaneous circulation was regained only by initial administration of epinephrine alone or in combination with Intralipid (®). Piglets receiving the combination therapy survived without further epinephrine support. In contrast, in groups 2 and 4, return of spontaneous circulation was only achieved after secondary epinephrine rescue.

In cardiac arrest caused by bupivacaine intoxication, first-line rescue with epinephrine and epinephrine + Intralipid (®) was more effective with regard to survival than Intralipid(®) alone and vasopressin + Intralipid(®) in this pig model (17).

Local anesthetic (LA) intoxication with severe hemodynamic compromise is a potential catastrophic event. Lipid resuscitation has been recommended for the treatment of LA-induced cardiac arrest. However, there are no data about effectiveness of Intralipid for the treatment of severe cardiovascular compromise prior to cardiac arrest. Aim of this study was to compare effectiveness of epinephrine and Intralipid for the treatment of severe Hemodynamic compromise owing to bupivacaine intoxication, anesthetized Piglets were with sevoflurane, intubated, and ventilated. Bupivacaine was infused with a syringe driver via a central venous catheter at a rate of 1 mg·kg−1·min−1 until invasively measured mean arterial pressure (MAP) dropped to 50% of the initial value. Bupivacaine infusion was then stopped, and epinephrine 3 μg·kg−1 (group 1), Intralipid (®) 20% 2 ml·kg−1 (group 2), or Intralipid 20% 4 ml·kg−1 (group 3) was immediately administered. Twenty-one piglets (3 × 7), were recorded. All animals in group 1 (100%) but only four of seven (57%) piglets in group 2 and group 3, respectively, survived. Normalization of hemodynamic parameters (HR, MAP) and ET (CO2) was fastest in group 1 with all piglets achieving HR and MAP values. hemodynamic compromise owing to bupivacaine intoxication in piglets, first-line rescue with epinephrine was more effective than Intralipid with regard to survival as well as normalization of hemodynamic parameters and ET (CO2) (18).

Intravenous lipid emulsion (ILE) has been proposed as a rescue therapy for severe local anesthetic drugs toxicity, but experience is limited with other lipophilic drugs. An 18-year-old healthy woman was admitted 8 h after the voluntary ingestion of sustained-release diltiazem (3600 mg), with severe hypotension refractory to fluid therapy, calcium salts, and high-dose norepinephrine (6.66 μg/kg/ min). Hyperinsulinemic euglycemia therapy was initiated and shortly after was followed by a protocol of ILE (intralipid 20%, 1.5 ml/kg as bolus, followed by 0.25 ml/kg over 1h). The main finding attributed to ILE was an apparent rapid decrease in insulin resistance, despite a prolonged serum diltiazem elimination half-life. Diltiazem is a lipophilic cardiotoxic drug, which could be sequestered in an expanded plasma lipid phase. The mechanism of action of ILE is not known, including its role in insulin resistance and myocardial metabolism in calcium-channel blocker poisoning (19).

Omega-6 Fatty Acids

Global beef production must increase in the next decades to meet the demands of a growing population, while promoting sustainable use of limited natural resources. Supplementing beef cattle with omega-6 fatty

acids (FAs) is a nutritional approach shown to enhance production efficiency, with research conducted across different environments and sectors of the beef industry. Omega-6 FA from natural feed ingredients such as soybean oil are highly susceptible to ruminal biohydrogenation. Hence, our and other research groups have used soybean oil in the form of Ca soaps (CSSO) to lessen ruminal biohydrogenation, and maximize delivery of omega-6 FA to the duodenum for absorption. In cow-calf systems, omega-6 FA supplementation to beef cows improved pregnancy success by promoting the establishment of early pregnancy. Cows receiving omega-6 FA during late gestation gave birth to calves that were healthier and more efficient in the feedlot, suggesting the potential role of omega-6 FA on developmental programming. Supplementing omega-6 FA to young cattle also elicited programming effects toward improved adipogenesis and carcass quality, and improved calf immunocompetence upon a stress stimulus. Cattle supplemented with omega-6 FA during growing or finishing periods also experienced improved performance and carcass quality. All these research results were generated using cattle of different genetic composition (*Bos taurus* and *B. indicus* influenced), and in different environments (tropical, subtropical, and temperate region). Hence, supplementing omega-6 FA via CSSO is a sustainable approach to enhance the production efficiency of beef industries across different areas of the world (20).

Prevention of murine influenza A virus pneumonitis

Non-ionic surfactant nano-emulsions have extensive anti-microbial activity and are biocompatible with skin and mucous membranes at effective concentrations. Two nano-emulsion formulations (8N8 and 20N10) made from soybean oil, tributyl phosphate and Triton X-100, were tested for their ability to prevent murine influenza virus pneumonia in vivo. In the initial study, CD-1 mice were administered various dilutions of the nano-emulsions intranasally, and safe dosages and concentrations were determined. Non-toxic concentrations of the nano-emulsions were then mixed with influenza virus and applied to the nares of mice. Animals receiving mixtures of two different emulsions (8N8 or 20N10) and a LD50 of virus survived the challenge without evidence of viral infection. To determine if the nano-emulsions could prevent influenza virus infection in vivo when used as a prophylactic treatment, the nano-emulsions (8N8 at 1.0% and 20N10 at 1.0% or 0.2%) were applied to mouse nares 90 min before exposure to 5x10(5) p.f.u./ml virus by nebulized aerosol. Animals pretreated with the nano-emulsions had significantly decreased clinical signs of infection. Only 26.0% (8N8 at 1.0%), 31.25% (20N10 at 1.0%) and 37.0% (20N10 at 0.2%) of animals pretreated with nano-emulsion died from pneumonitis, whereas >80.0% of mock pretreated animals succumbed to infection ($P<0.005$). These findings suggest that non-ionic surfactant nano-emulsions have therapeutic potential for the prevention of influenza virus infection in vivo (21).

In this study, investigations have been carried out to prepare adjuvant active delivery systems; multiple water-in-oil-in-water (w/o/w) emulsion formulations, containing influenza virus surface antigen Hemagglutinin (HA). A modified two-stage emulsification method has been used to prepare multiple emulsions. After improving multiple (w/o/w) emulsion formulations; F1: purified antigen solution (PAS)/soybean oil, HCO-40 and span 80/pluronic F-68, F2: PAS and HPbetaCD/soybean oil, HCO-40 and span 80/pluronic F-68, F3: PAS/squalane, HCO-40 and span 80/pluronic F-68, formulations were selected for the stability study that continued for a 3 month duration. To evaluate the stability of these formulations, microscopic observation, osmolarities of the internal and external aqueous phases, pH, globule size and viscosity were determined. SDS-PAGE (silver staining) was used to evaluate HA and the micro-bicinchoninic acid (mBCA) assay was used to determine the in vitro release of antigen from formulations. Immune responses of formulations were investigated in Wistar Albino rats and compared with the immune response raised against the conventional vaccine. These responses were detected with Hemagglutination Inhibition (HAI) assay. The results of this study demonstrated that HA was well entrapped in the multiple (w/o/w) emulsion formulations. Molecular weight and antigenicity of the entrapped HA were not affected by the emulsification procedure. These results suggest that multiple emulsion formulations entrapping influenza antigen may have potential for immunization studies as one of the vaccine delivery system with adjuvant properties (22).

Control of virus diseases in soybeans

Soybean, one of the world's most important sources of animal feed and vegetable oil, can be infected by numerous viruses. However, only a small number of the viruses that can potentially infect soybean are considered as major economic problems to soybean production. Therefore, we consider management options available to control diseases caused by eight viruses that cause, or have the potential to cause, significant economic loss to producers. We summarize management tactics in use and suggest direction for the future. Clearly, the most important tactic is disease resistance. Several resistance genes are available for three of the eight viruses discussed. Other options include use of virus-free seed and avoidance of alternative virus hosts when planting. Attempts at arthropod vector control have generally not provided consistent disease management. In the future, disease management will be considerably enhanced by knowledge of the interaction

between soybean and viral proteins. Identification of genes required for soybean defense may represent key regulatory hubs that will enhance or broaden the spectrum of basal resistance to viruses. It may be possible to create new recessive or dominant negative alleles of host proteins that do not support viral functions but perform normal cellular function. The future approach to virus control based on gene editing or exploiting allelic diversity points to necessary research into soybean-virus interactions. This will help to generate the knowledge needed for rational design of durable resistance that will maximize global production (23).

Mixed oil intravenous lipid emulsion (MO ILE) that contains 30% soybean oil (SO), 30% medium chain triglycerides, 25% olive oil and 15% fish oil can benefit hospitalized patients receiving parenteral nutrition (PN) but there are very few studies on its long-term use. Our goal was to evaluate the clinical outcomes of adults receiving home PN (HPN) with MO versus those receiving SO ILE over a 2-year period.

This is a retrospective analysis of data collected prospectively from a cohort of patients recorded in the Canadian HPN Registry over a 2-year period. HPN patients from academic programs across Canada were entered in the Registry according to a validated protocol. For this study, demographic, nutritional, laboratory and clinical data were extracted from January 1st 2015, when MO lipid emulsion became available in Canada, to July 24th 2019. Clinical data for each patient included: number of hospitalizations, number of hospitalizations related to HPN and number of hospitalization days related to HPN, over a year; incidence of line sepsis per 1000 catheter days and mortality. Data are presented as median (1st, 3rd quartile) for continuous variables and frequency (percentage) for categorical variables. Comparisons between groups were performed using two sample t-test or Wilcoxon Rank Sum tests for continuous variables and Chi-square tests or Fisher's exact tests for categorical variables. Univariate and multiple linear regressions were also carried out. Statistical significance is set at a p-value <0.05.

A total of 120 patients were included (MO n = 68, SO n = 52). Significant differences at baseline between the two groups were a higher use of Hickman line (62.12% vs 42%, p = 0.038) and more western Canada based hospital care with MO (75% vs 42.31%, p = 0.0002). The MO group had significantly more hospitalizations (p = 0.001), more hospitalizations related to HPN (p = 0.012) and more hospitalization days related to HPN (p = 0.016) per patient per year compared to SO patients. There was no significant difference between groups for line sepsis per 1000 catheter days (MO: 0.05 (0.0, 1.0) vs SO: 0.0 (0.0, 0.22), p = 0.053) or mortality. All other variables, including biochemical variables, were similar between groups. In a multiple regression analysis, the following factors were significantly associated with a greater number of hospitalizations per patient per year: use of MO, high blood glucose from the last recorded value and having died by the end of the study period.

This 2-year prospective cohort study suggests an increased risk of hospitalization in HPN patients receiving MO lipid emulsion. The long-term effect of using MO lipid emulsion in HPN patients should be further evaluated using a large randomized controlled trial. THE STUDY WAS REGISTERED IN CLINICALTRIALS.GOV: (NCT02299466) (24).

Given that micelles of lipids are colloids, the hypothesis was generated that the rapid administration of large volumes of soybean oil micelles would be an effective perfusion fluid. We also hypothesized that oxygen loading would be enhanced due to the greater solubility of oxygen in lipids compared to water.

A 100% lethal mouse model of blood loss was used to compare the ability of soybean oil micelles to that of Ringer's lactate, blood and other fluids, with respect to raising and maintaining the blood pressure for one hour. Oxygen on- and off-loading of various concentrations of soybean oil micelles was determined using mass spectroscopy. Nitric oxide uptake by micelles was also determined in a similar fashion.

A 20% soybean oil emulsion was superior to Ringer's lactate in raising and maintaining blood pressure. A 20% soybean oil emulsion with 5% albumin added was superior to shed blood as well as solutions comprised of 5% albumin added to either normal saline or Ringer's lactate. There was a linear relationship between oxygen content and micelle concentration between 10% and 30%. Off-loading of oxygen from the micelles was nearly as fast as off-loading from water. Nitric oxide also loaded preferentially onto soybean oil micelles.

(1) Soybean oil emulsions were superior to other fluids in restoring and maintaining the blood pressure; (2) oxygen-carrying ability of soybean oil micelles exceeds that of water and follows Henry's law between 10% and 30% w/v oil content; (3) nitric oxide was carried by the micelles; (4) animals receiving soybean oil micelles did not exhibit fat embolization; (5) colloids comprised of soybean oilcontaining micelles may be used to replace blood loss and may be used to deliver oxygen and other potentially therapeutic gases such as nitric oxide to tissues (25).

Cardiac protein changes in rats after soybean oil treatment

Several studies show that the consumption of vegetable oils, such as soybean oil, rich in polyunsaturated fatty acids (PUFAs) has beneficial health effects by preventing or reducing the risk factors of cardiovascular diseases. While the demonstration of beneficial effects of the consumption of unsaturated fatty

acids on the cardiovascular system has been proven in a macroscopic level, the molecular/cellular mechanisms responsible for this phenomenon are poorly understood.

In this work, a comparative proteomic approach, two-dimensional gel electrophoresis (2-DE) coupled to mass spectrometry (MALDI-TOF/TOF), was applied to investigate proteome differences in the left ventricle (LV) of rats that received 0.1 mL of soybean oil intramuscularly for 15 days (treated group-TR) and rats that had not (control group-CT).

Soybean oil treatment improved left ventricular function, TR animals presented lower value of LVEDP and significantly changed LV proteome. The protein profile of VE revealed differences in the expression of 60 protein spots ($p<0.05$) between the experimental groups (CT and TR), 14 of those were identified by MS and MS/MS, and 12 of the 14 being non-redundant proteins. Robust changes were detected in proteins involved in cellular structure and antioxidant system and muscular contraction.

The TR group presented an increase in the intensity of proteins involved in muscle contraction (myosin light chain-3 (3-MCL), creatine kinase M (CKM)) and thireodoxin, an antioxidant enzyme. Low intensity cytoskeletal protein, desmin, was also detected in TR animals. The results suggest that soybean oil induces changes in the levels of heart proteins which may partially account for the underlying mechanisms involved in the benefits provided by oils rich in polyunsaturated fatty acids (26).

A novel, killed-virus nasal vaccinia virus vaccine

Live-virus vaccines for smallpox are effective but have risks that are no longer acceptable for routine use in populations at minimal risk of infection. We have developed a mucosal, killed-vaccinia virus (VV) vaccine based on antimicrobial nanoemulsion (NE) of soybean oil and detergent. Incubation of VV with 10% NE for at least 60 min causes the complete disruption and inactivation of VV. Simple mixtures of NE and VV (Western Reserve serotype) (VV/NE) applied to the nares of mice resulted in both systemic and mucosal anti-VV immunity, virus-neutralizing antibodies, and Th1-biased cellular responses. Nasal vaccination with VV/NE vaccine produced protection against lethal infection equal to vaccination by scarification, with 100% survival after challenge with 77 times the 50% lethal dose of live VV. However, animals protected with VV/NE immunization did after virus challenge have clinical symptoms more extensive than animals vaccinated by scarification. VV/NE-based vaccines are highly immunogenic and induce protective mucosal and systemic immunity without the need for an inflammatory adjuvant or infection with live virus (27).

Soybean seeds

Soybean seeds possess several inherent qualities that make them an ideal host for the production of biopharmaceuticals when compared with other plant-based and non-plant-based recombinant expression systems (e.g., low cost of production, high protein to biomass ratio, long-term stability of seed proteins under ambient conditions, etc.). To demonstrate the practicality and feasibility of this platform for the production of subunit vaccines, we chose to express and characterize a nontoxic form of S. aureus enterotoxin B (mSEB) as a model vaccine candidate. We show that soy-mSEB was produced at a high vaccine to biomass ratio and represented ~76 theoretical doses of human vaccine per single soybean seed. We localized the model vaccine candidate both intracellularly and extracellularly and found no difference in mSEB protein stability or accumulation relative to subcellular environment. We also show that the model vaccine was biochemically and immunologically similar to native and recombinant forms of the protein produced in a bacterial expression system. Immunization of mice with seed extracts containing mSEB mounted a significant immune response within 14 days of the first injection. Taken together, our results highlight the practicality of soybean seeds as a potential platform for the production of functional subunit vaccines (28).

Plants have been identified as promising expression systems for commercial production of vaccine antigens. In phase I clinical trials several plant-derived vaccine antigens have been found to be safe and induce sufficiently high immune response. Thus, transgenic plants, including edible plant parts are suggested as excellent alternatives for the production of vaccines and economic scale-up through cultivation. Improved understanding of plant molecular biology and consequent refinement in the genetic engineering techniques have led to designing approaches for high level expression of vaccine antigens in plants. During the last decade, several efficient plant-based expression systems have been examined and more than 100 recombinant proteins including plant-derived vaccine antigens have been expressed in different plant tissues. Estimates suggest that it may become possible to obtain antigen sufficient for vaccinating millions of individuals from one acre crop by expressing the antigen in seeds of an edible legume, like peanut or soybean. In the near future, a plethora of protein products, developed through 'naturalized bioreactors' may reach market. Efforts for further improvements in these technologies need to be directed mainly towards validation and applicability of plant-based standardized mucosal and edible vaccines, regulatory pharmacology, formulations and the development of commercially viable GLP protocols. This article reviews the current status of developments in the area of use of plants for the development of vaccine antigens (29).

Soybean-derived vaccine

In an effort to develop a sustainable platform for manufacturing protein-based vaccine candidates, we expressed a triple mutant of staphylococcal enterotoxin B carrying the L45R, Y89A, and Y94A modifications in transgenic soybean seeds (soy-mSEB). Soy-mSEB possessed no detectable superantigen activity in vitro. We found that this soybean-derived, nontoxic mutant of SEB could be stably expressed, stored in seeds for extended periods at room temperature without degradation, and easily purified from contaminating soy proteins. Vaccination of pigs with purified soy-mSEB, or the identical triple mutant expressed in Escherichia coli (E. coli-mSEB), resulted in high antibody titers against the native toxin in immunized animals. In fact, titers were indistinguishable regardless of the immunogen used, demonstrating the equivalence of soy-mSEB and E. coli-mSEB vaccinations. Antisera from either immunized group were able to block native SEB superantigen activity in an in vitro neutralization assay. Similar results were obtained when immunized animals were challenged with a sublethal dose of native toxin. Significant reductions in toxin-induced serum cytokine levels were observed in soy-mSEB- and E. coli-mSEB-immunized pigs compared to control animals. The reductions in SEB-induced cytokine responses were similar regardless of the immunogen used for vaccination. Surprisingly, however, some clinical symptoms, such as prostration, lethargy, emesis, and/or diarrhea, were still observed in all immunized animals. These studies demonstrate the potential for soybeanderived proteins as a platform technology for sustainable vaccine manufacturing and the usefulness of a sublethal challenge model in pigs for evaluating the efficacy of potential SEB vaccine candidates (30).

A lipid based multi-compartmental system

The gastric mucosa provides the entry point for the majority of pathogens, as well as being the induction site for protective immunity; however, there remain few examples of oral vaccines due to the challenges presented by the gastrointestinal route. In this study, we develop a lipid-based multicompartmental system for oral vaccine delivery. Specifically, we have optimised the formulation of a water-in-oil-in-water double emulsion prepared from a triglyceride - soya bean oil, using surfactants

Span 80/Tween 80 and Pluronic F127 to stabilise the internal and external water phases, respectively. Into the internal water phase, we also incorporated a PEGylated liposome, prepared using hydrogenated phosphatidyl choline as a carrier for our model protein, FITC-labelled ovalbumin. We demonstrated the successful incorporation of intact liposomes into the internal water phase of the double emulsion using imaging techniques including cryo-SEM and confocal microscopy. Finally, we use in vitro release studies of FITC-ovalbumin, to provide further confirmation of the multi-compartmental structure of the double emulsion system and demonstrate significant extended release of the entrapped model antigen compared with PEG-liposomes; these characteristics are attractive for oral vaccine delivery (31).

Soybean RNA interference lines

Soybean mosaic virus (SMV), a potyvirus, is the most prevalent and destructive viral pathogen in soybean-planting regions of China. Moreover, other potyviruses, including bean common mosaic virus (BCMV) and watermelon mosaic virus (WMV), also threaten soybean farming. The eukaryotic translation initiation factor 4E (eIF4E) plays a critical role in controlling resistance/susceptibility to potyviruses in plants. In the present study, much higher SMV-induced eIF4E1 expression levels were detected in a susceptible soybean cultivar when compared with a resistant cultivar, suggesting the involvement of eIF4E1 in the response to SMV by the susceptible cultivar. Yeast two-hybrid and bimolecular fluorescence complementation assays showed that soybean eIF4E1 interacted with SMV VPg in the nucleus and with SMV NIa-Pro/NIb in the cytoplasm, revealing the involvement of VPg, NIa-Pro, and NIb in SMV infection and multiplication. Furthermore, transgenic soybeans silenced for eIF4E were produced using an RNA interference approach. Through monitoring for viral symptoms and viral titers, robust and broad-spectrum resistance was confirmed against five SMV strains (SC3/7/15/18 and SMV-R), BCMV, and WMV in the transgenic plants. Our findings represent fresh insights for investigating the mechanism underlying eIF4E-mediated resistance in soybean and also suggest an effective alternative for breeding soybean with broad-spectrum viral resistance (32).

Fatty acids, lipid emulsions and the immune and inflammatory systems

Fatty acids modulate the responses of cells of the immune system. Inflammatory and immune responses in patients receiving parenteral nutrition may be modulated by the type of lipid used, which may influence clinical outcomes. Lipid emulsions based solely upon soybean oil may not be optimal because of the role of n-6 fatty acids in promoting inflammation and suppressing immune responses. Lipid emulsions with soybean oil in various combinations with medium-chain triglycerides (MCTs), olive oil and fish oil are available. Some early studies have suggested better immune function with MCTsoybean oil than with soybean oil alone, but the differences were small, and more recent studies suggested little difference between soybean oil, MCT-soybean oil and soybean oil-olive oil regarding markers of inflammation and immunity. The inclusion

of fish oil in combination with one or more other oils (i.e. soybean, MCT, olive) in the parenteral regimen administered to patients following major gastrointestinal surgery reduces the post-surgery rise in inflammatory markers and the fall in cellmediated immune markers. These changes are associated with improvements in clinical outcomes. Whether similar effects of intravenous fish oil occur in critically ill patients is not clear at present because of the small number, small size and variable findings of existing studies. The lipid component of parenteral nutrition may modify inflammatory and immune processes in ways that influence patient outcome. The inclusion of fish oil in parenteral nutrition for post-surgical patients is associated with benefits. The situation regarding critically ill patients is not clear (33).

Nanoemulsion as an Adjuvant for an Inactivated H3N2 Influenza Vaccine

Adjuvant can reduce vaccine dosage and acquire better immune protection to the body, which helps to deal with the frequent outbreaks of influenza. Nanoemulsion adjuvants have been proved efficient, but the relationship between their key properties and the controlled release which greatly affects immune response is still unclear. The present work explores the role of factors such as particle size, the polydispersity index (PDI), stability and the safety of nanoemulsions by optimizing the water concentration, oil phase and modes of carrying, to explain the impact of those key factors above on adjuvant effect.

Isopropyl myristate (IPM), white oil, soybean oil, and grape-kernel oil were chosen as the oil phase to explore their roles in emulsion characteristics and the adjuvant effect. ICR mice were immunized with an emulsion-inactivated H3N2 split influenza vaccine mixture, to compare the nanoemulsion's adjuvant with traditional aluminium hydroxide or complete Freund's adjuvant.

Particle size of all the nanoemulsion formed in our experiment ranged from 20 nm to 200 nm and did not change much when diluted with water, while the PDI decreased obviously, indicating that the particles tended to become more dispersive. Formulas with 80% or 85.6% water concentration showed significant higher HAI titer than aluminium hydroxide or complete Freund's adjuvant, and adsorption rather than capsule mode showed higher antigen delivery efficiency. As mentioned about oil phase, G (IPM), F (white oil), H (soybean oil), and I (grape-kernel oil) showed a decreasing trend in their adjuvant efficiency, and nanoemulsion G was the best adjuvant with smaller and uniform particle size.

Emulsions with a smaller, uniform particle size had a better adjuvant effect, and the adsorption mode was generally more efficient than the capsule mode. The potential adjuvant order of the different oils was as follows: IPM > white oil > soybean oil > grape-kernel oil (34).

Oral intralipid emulsion use

We aimed to investigate whether oral intralipid emulsion (OIE) reduces pancreatic β-cell injury (PβCI) by chelating with malathion (M), or increases PβCI by increasing M absorption in the stomach. Fifty rats were randomly divided into six groups: control group (C); OIE administered group (L); Mtreated group (M); OIE-administered group immediately after given M (M0L); OIE-administered group 6 hours after being given M (M6L) and OIE administered group 12 hours after being given M (M12L). M induced PβCI, hyperglycemia, temporary hyperinsulinemia and oxidative stress (OS). However, there was no significant difference in serum levels of glucose, insulin, total oxidants (TOS) and liver TOS between the M0L group and groups C and L. Also, insulin levels of M12L significantly increased, compared to the M6L group. Biochemical results, which were confirmed by histopathology, indicate that administering OIE after 6 hours and immediately after taking M may markedly prevent PβCI, hyperglycemia and OS. In addition, OIE's effectiveness decreased after 6 hours and was totally ineffective after 12 hours. We concluded that OIE may help to achieve a better prognosis and reduce mortality rate in cases presented to the emergency department, particularly within the first 6 hours, resulting from organophosphate pesticide poisoning by oral ingestion (35).

The spectrum of lipid-induced changes in the secretion of hormones important in energy homeostasis has not yet been fully elucidated.

To identify potential incretin-like effects in response to lipid administration, we examined the shortterm effect of iv vs oral lipids on key molecules regulating energy homeostasis. Design, Intervention, and Participants: After a 10-hour overnight fast, 26 subjects were randomized to receive an oral lipid load, a 10% iv lipid emulsion, a 20% iv lipid emulsion, or an iv saline infusion. We obtained blood samples at 30-minute intervals for the first 2 hours and hourly thereafter for a total of 6 hours.

Circulating levels of insulin, glucose, c-peptide, free fatty acids, incretins (glucagon-like peptide-1, gastric inhibitory polypeptide), glucagon, peptide YY, ghrelin, fibroblast growth factor 21, fetuin A, irisin, omentin, and adiponectin were measured.

Oral lipid ingestion resulted in higher glucagon-like peptide-1, gastric inhibitory polypeptide, glucagon, and peptide YY levels, compared with the other three groups (incremental area under the curve $P = .003$, $P < .001$, $P < .001$, $P < .001$, respectively). The 20% lipid emulsion, leading to higher free fatty acid levels, resulted in greater insulin, c-peptide, and fibroblast growth factor 21 responses compared with placebo and the

other two groups (incremental area under the curve P = .002, P = .005, P < .001, P < .001, respectively). Omentin, adiponectin, fetuin A, and irisin levels were not affected by either mode of lipid administration.

II. Conclusions:

Metabolic responses to lipids depend on the route of administration. Only iv lipids trigger a dose-dependent fibroblast growth factor 21 secretion, which is nonglucagon mediated. Intravenous lipids also induce hyperinsulinemia without concurrent decreases in glucose, a phenomenon observed in insulin-resistant states. Orally administered lipids mostly affect gastrointestinal tract-secreted molecules important in glucose and energy homeostasis such as glucagon, incretins, and peptide YY (36).

Conclusion

Combined Covid 19 vaccine and daily oral Intralipid or soybean oil (main component of Intralipid) for the eradication of the Corona Pandemic is first suggested in the medical literature.

References

[1]. Ysrafil 1, Rosdiana Mus 2, NoviyantiIndjar Gama 3, DwiRahmaisyah 4, RiskahNur'amalia 5. Emerging Mutation in SARSCoV-2 Spike: Widening Distribution Over Time in Different Geographic Areas. Biomed J . 2021 Jul 13;S23194170(21)00090-1. https://www.linkedin.com/pulse/can-intralipid-lipid-emulsion-inactivate-coronavirus-someone-eldor/

[2]. Metabolite, Protein, and Lipid Extraction (MPLEx): A Method that Simultaneously Inactivates Middle East Respiratory

[3]. Syndrome Coronavirus and Allows Analysis of Multiple Host Cell Components Following Infection.Carrie D. Nicora, Amy C. Sims, Kent J. Bloodsworth, Young-Mo Kim, Ronald J. Moore, Jennifer E. Kyle, Ernesto S. Nakayasu, Thomas O. Metz. MERS Coronavirus pp 173-194. Part of the Methods in Molecular Biology book series (MIMB, volume 2099). First Online: 28 December 2019. https://link.springer.com/protocol/10.1007%2F978-1-0716-02119_14

[4]. Javid MJ1 * and Zebardast J2 1 Department of Anesthesiology, Farabi Hospital, Tehran University of Medical Sciences, Iran 2 PH. D Candidate of Cognitive Neuroscience Institute for Cognitive Science Studies (ICSS), Tehran, Iran *Corresponding author: Mihan J Javid, MD, Department of Anesthesiology, Farabi Hospital, Tehran University of Medical Sciences, Iran Received: April 26, 2020; Accepted: May 15, 2020; Published: May 22, 2020 Javid MJ and Zebardast J. Rescue Therapy by Intralipid in Covid 19 Pulmonary Complications: A Novel Approach. Austin J Anesthesia and Analgesia. 2020; 8(2): 1087.

[5]. Maria Vasilieva , Irina VasilievaIlieVasiliev, et al. Intralipid in the Target Treatment of Lipid Peroxidation Disorder Caused by Oxidative and Nitro- Galogenic Stress in Patients with SARS-Cov2 / COVID / 19. Journal of Advances in Medical and Pharmaceutical Sciences 2020 - Volume 22 [Issue 11] Page 20-30, Published: 31 December 2020

[6]. Russell, R.L. & Westfall, B.A., 1962. Alleviation of barbiturate depression. AnesthAnalg, 41(5), pp.582–585.

[7]. Krieglstein, J., Meffert, A. & Niemeyer, D., 1974. Influence of emulsified fat on chlorpromazine availability in rabbit blood. Experientia, 30(8), pp.924–926.

[8]. Straathof, D.J., Driessen, O., Meijer, J.W., Van Rees, H., Vermeij, P. &Vermeij, T.A., 1984. Influence of Intralipid infusion on the elimination of phenytoin. Arch Int PharmacodynTher, 267(2), pp.180–186.

[9]. Weinberg, G.L., VadeBoncouer, T., Ramaraju, G.A., Garcia-Amaro, M.F. &Cwik, M.J., 1998. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. Anesthesiology, 88(4), pp.1071–1075.

[10]. Weinberg, G., 2002. Current concepts in resuscitation of patients with local anesthetic cardiac toxicity. Reg Anesth Pain Med, 27(6), pp.568–575.

[11]. Cave, G. & Harvey, M., 2009a. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. AcadEmerg Med, 16(9), pp.815–824.

[12]. Rosenblatt, M.A., Abel, M., Fischer, G.W., Itzkovich, C.J. &Eisenkraft, J.B., 2006. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. Anesthesiology, 105(1), pp.217–218.

[13]. Minton, N.A., Goode, A.G. & Henry, J.A., 1987. The effect of a lipid suspension on amitriptyline disposition. Arch Toxicol, 60(6), pp.467–469.

[14]. Cave, G., Harvey, M. &Graudins, A., 2011. Review article: Intravenous lipid emulsion as antidote: A summary of published human experience. Emerg Med Australas, 23(2), pp.123–141.

[15]. A. Papadopoulou, J. W. Willers, T. L. Samuels and D. R. Uncles, "The Use of Dye Surrogates to Illustrate Local Anesthetic Drug Sequestration by Lipid Emulsion: A Visual Demonstration of the Lipid Sink Effect," Regional Anesthesia & Pain Medicine, Vol. 37, No. 2, 2012, pp. 183-187.

[16]. A. M. Grunbaum, B. M. Gilfix, S. Gosselin and D. W. Blank, "Analytical Interferences Resulting from Intravenous Lipid Emulsion," Clinical Toxicology (Phila), Vol. 50, No. 9, 2012, pp. 812-817.

[17]. J. Mauch, O. M. Jurado, N. Spielmann, R. BettschartWolfensberger and M. Weiss, "Resuscitation Strategies from Bupivacaine-Induced Cardiac Arrest," Pediatric Anesthesia, Vol. 22, No. 2, 2012, pp. 124-129.

[18]. J. Mauch, O. M. Jurado, N. Spielmann, R. BettschartWolfensberger and M. Weiss, "Comparison of Epinephrine vs Lipid Rescue to Treat Severe Local Anesthetic Toxicity—An Experimental Study in Piglets," Pediatric Anesthesia, Vol. 21, No. 11, 2011, pp. 1103-1108.

[19]. V. Montiel, T. Gougnard and P. Hantson, "Diltiazem Poisoning Treated with Hyperinsulinemic Euglycemia Therapy and Intravenous Lipid Emulsion," European Journal of Emergency Medicine, Vol. 18, No. 2, 2011, pp. 121-123.

[20]. Bruno IedaCappellozza 1, Reinaldo Fernandes Cooke 2, Kelsey Margaret Harvey 3. Omega-6 Fatty Acids: A Sustainable Alternative to Improve Beef Production Efficiency. Animals (Basel) . 2021 Jun 12;11(6):1764.

[21]. B W Donovan 1, J D Reuter, Z Cao, A Myc, K J Johnson, J R Baker Jr. Prevention of murine influenza A virus pneumonitis by surfactant nano-emulsions. Antivir Chem Chemother. 2000 Jan;11(1):41-9.

[22]. AsumanBozkir 1, GokhanHayta. Preparation and evaluation of multiple emulsions water-in-oil-in-water (w/o/w) as delivery system for influenza virus antigens. J Drug Target. 2004 Apr;12(3):157-64.

[23]. John H Hill 1, Steven A Whitham 2. Control of virus diseases in soybeans. Adv Virus Res. 2014;90:355-90.

[24]. Nayima M Clermont-Dejean 1, Katherine J P Schwenger 1, Ennaliza Salazar 2, FláviaFaganello Colombo 3, Zihang Lu 4, Wendy Lou 5, Leah Gramlich 6, Scott Whittaker 7, David Armstrong 8, Brian Jurewitsch 9, Maitreyi Raman 10, Donald R Duerksen 11, James D McHattie 12, Sanjay Murthy 13, Johane P Allard 14. Home parenteral nutrition patients on mixed oil lipid emulsion have a

higher rate of hospitalizations compare to those on soybean oil- a prospective 2-year cohort study. Clin Nutr. 2021 Jun 17;40(7):4616-4623

[25]. M Armbruster 1, E Grimley, J Rodriguez, D Nacionales, P Efron, L Moldawer, K Papadopoulos, R Ungaro, A Cuenca, C Simpkins. Soybean oil: a potentially new intravascular perfusate. Perfusion. 2013 Mar;28(2):160-6.

[26]. TaislaSoprani 1, Vinicius KufferUliana 2, Rogerio Faustino Ribeiro Jr 3, Sergio Lisboa Jr 4, Gabriella Xavier Maretto 5, André Teixeira Silva da Ferreira 6, Jonas Perales 7, IvanitaStefanon 8, Suely Gomes de Figueiredo 9. Cardiac protein changes in rats after soybean oil treatment: a proteomic study. Lipids Health Dis. 2015 Apr 14;14:26.

[27]. Anna U Bielinska 1, Alexander A Chepurnov, Jeffrey J Landers, Katarzyna W Janczak, Tatiana S Chepurnova, Gary D Luker, James R Baker Jr. A novel, killed-virus nasal vaccinia virus vaccine. Clin Vaccine Immunol. 2008 Feb;15(2):34858.

[28]. Laura C Hudson 1, Renu Garg 2, Kenneth L Bost 3, Kenneth J Piller 3. Soybean seeds: a practical host for the production of functional subunit vaccines. Biomed Res Int. 2014;2014:340804.

[29]. Siddharth Tiwari 1, Praveen C Verma, Pradhyumna K Singh, Rakesh Tuli. Plants as bioreactors for the production of vaccine antigens. Biotechnol Adv. Jul-Aug 2009;27(4):449-67.

[30]. Laura C Hudson 1, Brynn S Seabolt, Jack Odle, Kenneth L Bost, Chad H Stahl, Kenneth J Piller. Sublethal staphylococcal enterotoxin B challenge model in pigs to evaluate protection following immunization with a soybean-derived vaccine. Clin Vaccine Immunol. 2013 Jan;20(1):24-32.

[31]. JinJauLiau 1, Sarah Hook 2, Clive A Prestidge 3, Timothy J Barnes 4. A lipid based multi-compartmental system: Liposomes-in-double emulsion for oral vaccine delivery. Eur J Pharm Biopharm. 2015 Nov;97(Pt A):15-21.

[32]. Le Gao 1 2, Jinyan Luo 1, Xueni Ding 1, Tao Wang 1 3, Ting Hu 1, Puwen Song 1, Rui Zhai 1, Hongyun Zhang 1, Kai Zhang 1, Kai Li 1, HaijianZhi 1. Soybean RNA interference lines silenced for eIF4E show broad potyvirus resistance. Mol Plant Pathol. 2020 Mar;21(3):303-317.

[33]. Elizabeth A Miles 1, Philip C Calder. Fatty acids, lipid emulsions and the immune and inflammatory systems. World Rev Nutr Diet. 2015;112:17-30.

[34]. Lanhua Zhao 1 2, Zhe Zhu 1, Lei Ma 1, Yingbo Li 1.O/W Nanoemulsion as an Adjuvant for an Inactivated H3N2 Influenza Vaccine: Based on Particle Properties and Mode of Carrying. Int J Nanomedicine. 2020 Mar 25;15:2071-2083.

[35]. Kasim Tuzcu 1, Harun Alp, Tumay Ozgur, Murat Karcioglu, Isil Davarci, Osman Evliyaoglu, Ali Karakus, Sedat Hakimoglu. Oral intralipid emulsion use: a novel therapeutic approach to pancreatic β-cell injury caused by malathion toxicity in rats. Drug Chem Toxicol 2014 Jul;37(3):261-7.

[36]. Maria T Vamvini 1, Ole-Petter Hamnvik 1, Ayse Sahin-Efe 1, Anna Gavrieli 1, Fadime Dincer 1, Olivia M Farr 1, Christos S Mantzoros 1. Differential Effects of Oral and Intravenous Lipid Administration on Key Molecules .Related to Energy Homeostasis. J Clin Endocrinol Metab. 2016 May;101(5):1989-97

.

Joseph Eldor, MD. "Combined Covid 19 vaccine and DAILY oral Intralipid or Soybean oil (main component of Intralipid) for the eradication of the Corona Pandemic." *IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)*, 17(1), (2022): pp. 32-42.