OxyCarrier

OxyCarrier Inc.

Changing the world's transfusion medicine for animals with japanese technology!

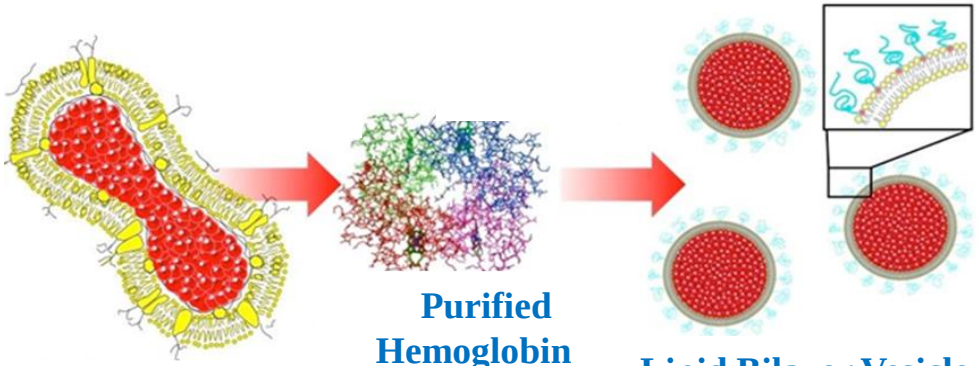
Artificial Red Blood Cells (ARBCs) for Animals （1）

Current status of blood transfusion in veterinary medicine

* Lack of a blood transfusion system
* Difficulty in securing donor animals
* Animal welfare issues on volunteer donation
* Inadequate blood typing technology
* Absolute lack of transfusion blood

* It is urgent to develop an artificial formulation (Artificial Red Blood Cells: ARBCs), ready-to-use when necessary.
* The raw material of our ARBCs is bovine blood in large quantities and at low cost.

Manufacturing process of ARBCs



Bovine Blood （5μm）

Purified Hemoglobin (Hb)（5nm）

Lipid Bilayer Vesicle （250nm）

Advantage of ARBCs

1) No blood type
2) No Pathogen
3) Long shelf life: Two years at room temperature
4) Biocompatibility
5) High oxygen transporting capacity
6) Low toxicity

* Collaborative research with Nara Medical University (Prof. Sakai)

OxyCarrier Inc. E-mail: info@oxycarrier.com

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ARBCs for Animals （2）

Efficacy and Safety : Suggestion from animal test data of ARBC using human blood

Efficacy data

1	80%-90% blood exchange, rats, hamsters	Recovery from hypotension, same with RBC
2	Shock resuscitation from 50% hemorrhage, rats, hamsters	Recovery from hypotension and anemia
3	Resuscitation from repeated 40% hemorrhage, rabbits	Reduction of inflammatory cytokine levels
4	Shock resuscitation from 50% hemorrhage, beagle dogs	Large animal, recovery from shock, survival
5	Prime fluid for extracorporeal circulation, rats	Brain function is preserved at hemodilution
6	Life saving at uncontrolled hemorrhage, rats	Prolonged survival time
7	Life saving at pulmonary resection, rats	Improved resuscitation and survival
8	Resuscitation from hemorrhagic shock, thrombocytopenic model, rats	Improved survival rate
9	Acute apnea during anesthesia, rats	Prolonged time until circulatory collapse
10	Brain infarction model, rats	Minimizing infarct size
11	Perfusion of isolated intestines	Intestinal function was preserved for > 2 hrs
12	Oxygenation of ischemic tissue in hamster skin flaps	Oxygen delivery through collateral arteries
13	Oxygenation of tumor for radiation therapy, rats	Reduction of tumor size
14	Placental hypoxia model, rats	Fetal oxygenation and growth were improved
15	Perfusion of amputated leg and replantation, rats	Successful replantation and function
16	Perfusion of isolated liver, pigs	Sustained oxygen consumption
17	Photosensitizer for port wine stain model, chicken wattle	Improved photocoagulation in capillaries
18	PET imaging of brain using $^{15}O_2$, rats	Brain metabolism image for detecting stroke
19	CO-HbV for shock resuscitation, rats	Reduced reperfusion injury
20	CO-HbV for pulmonary fibrosis, mice	Reduced fibrosis
21	CO-HbV for colitis, mice	Reduced inflammation
22	CO-HbV for acute pancreatitis, mice	Reduced inflammation
23	Combination therapy of artificial platelets & artificial red cells, rats	Improved survival from hemorrhagic shock

Safety data

1	Blood compatibility (human blood, rat, pig, beagles)	No or little influence on platelet function, complement system, and kinin system
2	General toxicity test after 40% blood exchange, rats	No irreversible changes in hematological, biochemical and histological observations
3	General toxicity test focusing on metabolic system after repeated massive injection (10 mL/kg/day x 14days), rats	Massive dosage (2.5 times of blood volume) induced transient splenohepatomegaly
4	Intra-cerebral hemorrhage model, rats	No influences on brain tissue repair
5	Biodistribution in rats, mice, and rabbits	Clarifying ADME. Half life in human is estimated as long as 3 days.
6	Biodistribution in rats with hepatic disorder	HbV is decomposed and excreted safely at hepatic disorder.
7	Immunological responses, rats	Transient suppression of cell-mediated immunity only in spleen
8	Resuscitation from hemorrhagic shock, rats	Absence of post-transfusion lung injury
9	Subcutaneous microcirculation, hamsters	No vasoconstriction, no hypertension
10	One-year observation, 40% shock resuscitation, beagles	One year survival, no organ damage
11	Toxicological test by single & repeated injection, Cynomolgus monkey	Safety confirmation
12	Toxicological test by single injection into pregnant rats	No placental transfer of Hb-V
13	Toxicological test by single injection into hyperlipidemic rats	No influence on Hb-V metabolism

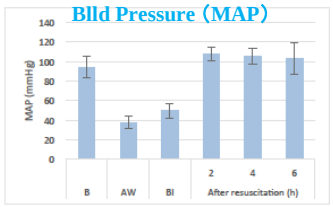
Efficacy and safety in beagle dogs : Suggested effect in dogs

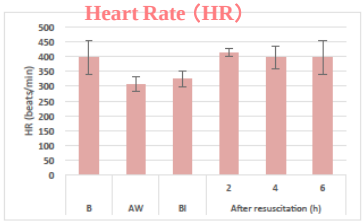
Biocompatibility in xenogenic animal : Suggested safety in Bovine Hb-vesicle

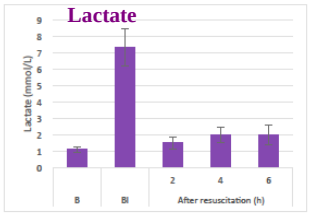
Fluid resuscitation with our ARBCs in acute hemorrhaged rats

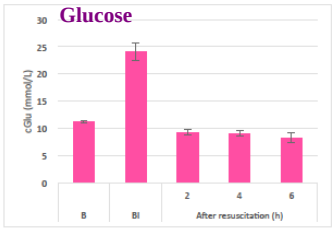
Methods: Rats were bled 50% of the total circulating blood volume, 15 minutes later BoHb-V was slowly administered and observed up to 6 hours later.

Results: Rats became shocked due to heavy bleeding and exhibited hypotension, low heart rate, high lactic acid blood, high glucose, etc., but almost recovered by administration of bovine artificial red blood cells (BoHb-V). This result was considered to be equivalent to that of human artificial red blood cells (HuHb-V).

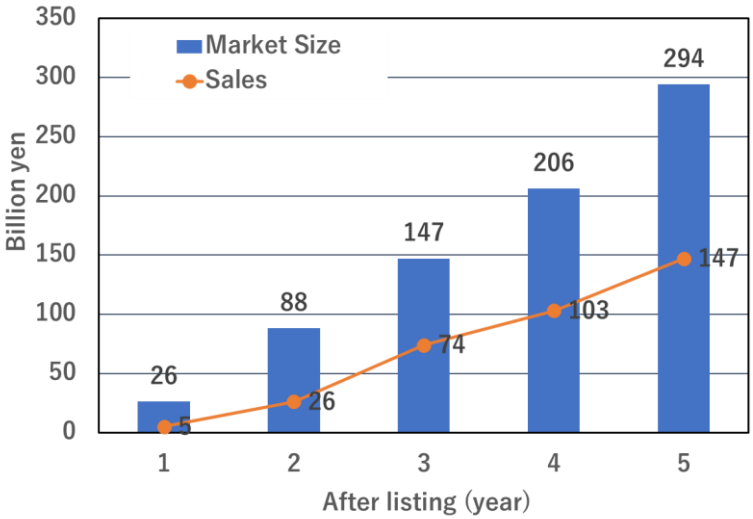








Japan transfusion market size and sales forecast（Dog）



After listing	Market size (Billion yen)	Sales
1year:	26	5
2years:	88	26
3years:	147	74
4years:	206	103
5years:	294	147

In dogs, 66% of all breeding populations are consulted, of which blood transfusions are 0.89% (2018 data), exploring large potential markets