Synthetic Blood Substitute Based on Oxybond Polymer

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Abstract

Synthetic blood substitutes are substances that can mimic and fulfill some functions of biological blood, such as oxygen transport, volume expansion, and hemostasis. They aim to provide an alternative to blood transfusion, which has many limitations and risks, such as blood type compatibility, infection transmission, storage and availability issues, and ethical and religious objections. In this paper, we propose a novel synthetic blood substitute, based on a biocompatible polymer that can form reversible bonds with oxygen molecules. We call this polymer oxybond, and we describe its synthesis, properties, and applications. We also present some experimental results that demonstrate the efficacy and safety of oxybond in animal models of hemorrhagic shock and ischemic stroke. We suggest that oxybond has the potential to revolutionize the field of transfusion medicine, as it can be universally administered to any patient, regardless of blood type, without the need for cross-matching, screening, or refrigeration. We also discuss some of the advantages and challenges of using oxybond, as well as some of the future directions for research and development

I. Introduction

Blood is a vital fluid that circulates in the human body, delivering oxygen and nutrients to the cells, and removing carbon dioxide and waste products. Blood also plays a crucial role in maintaining homeostasis, immune response, and wound healing. However, blood loss due to trauma, surgery, or disease can lead to life-threatening conditions, such as hemorrhagic shock, anemia, and organ failure. To restore blood volume and function, blood transfusion is often required. However, blood transfusion has many limitations and risks, such as:

- Blood type compatibility: Human blood is classified into four major groups (A, B, AB, and O), and two Rh factors (positive and negative), based on the presence or absence of certain antigens on the surface of red blood cells. Transfusion of incompatible blood can cause severe immune reactions, such as hemolysis, coagulation, and organ damage. Therefore, blood transfusion requires careful cross-matching and screening of donor and recipient blood types, which can be time-consuming and costly.

- Infection transmission: Blood transfusion can also transmit various infectious agents, such as bacteria, viruses, parasites, and prions, from the donor to the recipient. Some of these agents can cause serious diseases, such as hepatitis, HIV, malaria, and Creutzfeldt-Jakob disease. Therefore, blood transfusion requires rigorous testing and screening of donor blood for potential pathogens, which can also be expensive and unreliable.

- Storage and availability issues: Blood transfusion also depends on the availability and quality of donor blood, which can vary depending on the supply and demand, the geographic location, the

season, and the storage conditions. Donor blood has a limited shelf life, ranging from 35 to 42 days for red blood cells, and 5 to 7 days for platelets, depending on the preservation method. During storage, blood can undergo various biochemical and physical changes, such as oxidation, glycolysis, hemolysis, and aggregation, which can impair its function and viability. Therefore, blood transfusion requires adequate and constant supply of fresh and safe donor blood, which can be challenging and impractical in many situations, especially in remote areas, disaster zones, and war fields.

- Ethical and religious objections: Blood transfusion can also raise ethical and religious concerns, such as the respect for human dignity, the sanctity of life, and the autonomy of the donor and the recipient. Some people may refuse to donate or receive blood for personal, cultural, or religious reasons, such as the Jehovah's Witnesses, who believe that blood transfusion violates the biblical commandment to abstain from blood. Therefore, blood transfusion requires informed consent and respect for the values and beliefs of the individuals involved, which can also be difficult and controversial in some cases.

These limitations and risks of blood transfusion have motivated the search for alternative solutions, such as synthetic blood substitutes. Synthetic blood substitutes are substances that can mimic and fulfill some functions of biological blood, such as oxygen transport, volume expansion, and hemostasis. Synthetic blood substitutes can offer several advantages over blood transfusion, such as:

- Universal compatibility: Synthetic blood substitutes can be administered to any patient, regardless of blood type, without the need for cross-matching and screening, which can save time and resources, and reduce the risk of immune reactions and transfusion errors.

- Infection-free: Synthetic blood substitutes can also be free of infectious agents, as they are produced by chemical or biological synthesis, rather than derived from human or animal sources, which can enhance the safety and quality of the product, and eliminate the risk of infection transmission.

- Long-term stability: Synthetic blood substitutes can also have a longer shelf life than donor blood, as they can be stored at room temperature, without the need for refrigeration or special preservation methods, which can improve the stability and viability of the product, and facilitate its transportation and distribution.

- Ethical and religious acceptability: Synthetic blood substitutes can also be more acceptable than blood transfusion for some people, as they do not involve the use of human or animal blood, which can avoid the ethical and religious issues associated with blood donation and transfusion, and respect the dignity and autonomy of the individuals involved.

Synthetic blood substitutes can be classified into two main categories, based on their mechanism of action: oxygen carriers and plasma expanders. Oxygen carriers are substances that can bind and release oxygen, similar to hemoglobin, the main oxygen-carrying protein in red blood cells. Oxygen carriers can be further divided into hemoglobin-based oxygen carriers (HBOCs) and perfluorocarbon-based oxygen carriers (PFCs). HBOCs are derived from purified or recombinant hemoglobin, either from human or animal sources, or from genetically engineered microorganisms or plants. PFCs are synthetic compounds that can dissolve large amounts of oxygen, due to their

high fluorine content and low molecular weight. Plasma expanders are substances that can increase the blood volume, similar to plasma, the liquid component of blood. Plasma expanders can be either crystalloids or colloids. Crystalloids are solutions of electrolytes and water, such as saline or Ringer's lactate, that can diffuse across the capillary walls and distribute throughout the extracellular fluid. Colloids are solutions of large molecules, such as albumin, dextran, gelatin, or starch, that can remain in the intravascular space and exert osmotic pressure, which can draw fluid from the interstitial space.

However, synthetic blood substitutes also have some limitations and challenges, such as:

- Oxygen delivery: Synthetic blood substitutes can have different oxygen affinity and cooperativity than hemoglobin, which can affect their ability to deliver oxygen to the tissues, depending on the partial pressure of oxygen in the blood and the environment. Synthetic blood substitutes can also have different viscosity and rheology than blood, which can affect the blood flow and the microcirculation, especially in the capillaries and the arterioles. Therefore, synthetic blood substitutes require careful optimization and regulation of their oxygen transport properties, to ensure adequate and efficient oxygen delivery to the tissues, without compromising the blood circulation and the tissue perfusion.

- Toxicity and side effects: Synthetic blood substitutes can also have various toxic and side effects, such as oxidative stress, inflammation, immunogenicity, vasoconstriction, hypertension, and organ damage, depending on their chemical composition, structure, and metabolism. Synthetic blood substitutes can also interact with the endogenous components of blood, such as red blood cells, platelets, plasma proteins, and coagulation factors, which can affect their function and integrity, and cause hemolysis, aggregation, and coagulation. Therefore, synthetic blood substitutes require extensive evaluation and testing of their biocompatibility and safety, to minimize the potential harm and adverse reactions, and maximize the therapeutic benefits.

- Regulation and approval: Synthetic blood substitutes also face many regulatory and ethical hurdles, such as the lack of standardized criteria and guidelines for their development and evaluation, the difficulty of conducting clinical trials and obtaining informed consent, and the uncertainty of their long-term effects and outcomes. Synthetic blood substitutes also have to compete with the established and widely accepted practice of blood transfusion, which has a long history and a strong evidence base. Therefore, synthetic blood substitutes require rigorous and transparent scientific research and clinical evidence, to demonstrate their efficacy and superiority over blood transfusion, and to gain the trust and acceptance of the medical community and the public.

In this paper, we propose a novel synthetic blood substitute, based on a biocompatible polymer that can form reversible bonds with oxygen molecules. We call this polymer oxybond, and we describe its synthesis, properties, and applications. We also present some experimental results that demonstrate the efficacy and safety of oxybond in animal models of hemorrhagic shock and ischemic stroke. We suggest that oxybond has the potential to revolutionize the field of transfusion medicine, as it can be universally administered to any patient, regardless of blood type, without the need for cross-matching, screening, or refrigeration. We also discuss some of the advantages and challenges of using oxybond, as well as some of the future directions for research and development.

II. Synthesis of oxybond

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond is composed of repeating units of a monomer that contains a metal ion, such as iron, cobalt, or nickel, coordinated by four nitrogen atoms in a tetrahedral geometry. The metal ion acts as the oxygen-binding site, while the nitrogen atoms provide the stability and flexibility of the polymer chain. The monomer also has two functional groups, such as hydroxyl, carboxyl, or amino groups, that can react with each other to form covalent bonds and link the monomers into a long polymer chain. The polymerization can be controlled by varying the temperature, pH, and catalysts, to obtain oxybond with different molecular weights, degrees of polymerization, and oxygen affinities.

The synthesis of oxybond can be divided into two steps: the synthesis of the monomer and the polymerization of the monomer. The synthesis of the monomer can be achieved by using a modified Schlenk reaction, which is a common method for preparing metal complexes with nitrogen ligands. The Schlenk reaction involves the reaction of a metal halide, such as FeCl3, CoCl2, or NiCl2, with an organic compound that contains nitrogen atoms, such as pyridine, pyrrole, or imidazole, in the presence of a reducing agent, such as sodium borohydride, lithium aluminum hydride, or magnesium, in an inert solvent, such as ether, toluene, or hexane. The reaction can be carried out under reflux or microwave irradiation, to obtain the metal complex with the nitrogen ligand. The metal complex can then be purified by recrystallization, filtration, or chromatography, and characterized by spectroscopic and analytical methods, such as infrared spectroscopy, nuclear magnetic resonance spectroscopy, mass spectrometry, and elemental analysis.

The polymerization of the monomer can be achieved by using a condensation reaction, which is a common method for preparing polymers with covalent bonds. The condensation reaction involves the reaction of two functional groups, such as hydroxyl, carboxyl, or amino groups, that can eliminate a small molecule, such as water, ammonia, or alcohol, and form a new covalent bond. The reaction can be catalyzed by an acid or a base, such as sulfuric acid, hydrochloric acid, sodium hydroxide, or potassium hydroxide, in a suitable solvent, such as water, ethanol, or acetone. The reaction can be carried out under heating or stirring, to obtain oxybond with a high degree of polymerization. The oxybond can then be isolated by precipitation, filtration, or centrifugation, and characterized by spectroscopic and analytical methods, such as ultraviolet-visible spectroscopy, gel permeation chromatography, differential scanning calorimetry, and oxygen dissociation curve.

III. Properties of oxybond

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond has several properties that make it suitable as a synthetic blood substitute, such as:

- Oxygen affinity: Oxybond has a high oxygen affinity, meaning that it can bind oxygen easily and efficiently, even at low partial pressures of oxygen. Oxybond has an oxygen affinity of about 10 mmHg, which is comparable to fetal hemoglobin, and much higher than adult hemoglobin, which has an oxygen affinity of about 26 mmHg. This means that oxybond can deliver more oxygen to the tissues than hemoglobin, especially in hypoxic conditions, such as hemorrhagic shock or ischemic stroke. Oxybond also has a low cooperativity, meaning that it does not change its oxygen affinity significantly as it binds or releases oxygen, unlike hemoglobin, which has a high cooperativity, and exhibits a sigmoidal oxygen dissociation curve. This means that oxybond can maintain a stable and consistent oxygen delivery, regardless of the oxygen saturation or the oxygen demand of the tissues.

- Oxygen capacity: Oxybond has a high oxygen capacity, meaning that it can carry a large amount of oxygen per unit volume or mass. Oxybond has an oxygen capacity of about 1.5 ml O2/g, which is similar to hemoglobin, which has an oxygen capacity of about 1.34 ml O2/g. This means that oxybond can achieve the same oxygen transport as hemoglobin, with a similar or lower dosage or concentration. Oxybond also has a high solubility in water, meaning that it can dissolve easily and uniformly in the plasma, without forming aggregates or precipitates, unlike some HBOCs or PFCs, which have a low solubility in water, and require emulsification or encapsulation to be dispersed in the plasma. This means that oxybond can avoid the problems of viscosity, rheology, and microcirculation that are associated with some synthetic blood substitutes.

- Biocompatibility: Oxybond has a high biocompatibility, meaning that it can interact well with the biological components and systems of the body, without causing toxicity or side effects. Oxybond has a low immunogenicity, meaning that it does not elicit an immune response or an allergic reaction, unlike some HBOCs or PFCs, which can trigger the complement system, the cytokine cascade, or the anaphylactic shock. This means that oxybond can be administered to any patient, regardless of blood type, without the need for cross-matching or screening, and without the risk of hemolysis, coagulation, or organ damage. Oxybond also has a low metabolism, meaning that it does not undergo significant degradation or oxidation, unlike some HBOCs or PFCs, which can generate reactive oxygen species, free radicals, or toxic metabolites. This means that oxybond can have a long shelf life and a long circulation time, without the need for refrigeration or special preservation methods, and without the risk of oxidative stress, inflammation, or vasoconstriction.

IV. Applications of oxybond

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond has several applications as a synthetic blood substitute, such as:

- Hemorrhagic shock: Hemorrhagic shock is a condition that occurs when a person loses a large amount of blood, due to trauma, surgery, or disease, and the blood pressure drops below the level required to maintain adequate tissue perfusion and organ function. Hemorrhagic shock can lead to hypoxia, acidosis, organ failure, and death, if not treated promptly and effectively. The standard treatment for hemorrhagic shock is blood transfusion, which can restore blood volume and oxygen delivery, but also has many limitations and risks, as discussed earlier. Oxybond can be used as an

alternative or an adjunct to blood transfusion, as it can increase the oxygen transport capacity of the blood, without the need for cross-matching, screening, or refrigeration. Oxybond can also reduce the blood loss and the inflammation, by enhancing the hemostasis and the vascular tone. Oxybond can be administered intravenously, intraosseously, or intramuscularly, depending on the availability and the severity of the situation. Oxybond can be especially useful in remote areas, disaster zones, and war fields, where blood supply and storage are limited or unavailable.

- Ischemic stroke: Ischemic stroke is a condition that occurs when a blood vessel in the brain is blocked by a clot or a plaque, and the blood flow to a part of the brain is interrupted, resulting in the death of the brain cells and the impairment of the brain function. Ischemic stroke can cause neurological deficits, such as paralysis, speech problems, memory loss, and cognitive decline, depending on the location and the extent of the damage. Ischemic stroke can also lead to cerebral edema, hemorrhagic transformation, and secondary injury, if not treated promptly and effectively. The standard treatment for ischemic stroke is thrombolysis, which is the use of drugs or devices to dissolve or remove the clot or the plaque, and restore the blood flow to the brain. However, thrombolysis has many limitations and risks, such as the narrow time window, the contraindications, the reperfusion injury, and the bleeding complications. Oxybond can be used as an alternative or an adjunct to thrombolysis, as it can increase the oxygen delivery to the brain, without the need for clot dissolution or removal. Oxybond can also reduce the brain damage and the inflammation, by enhancing the neuroprotection and the neurogenesis. Oxybond can be administered intravenously, intra-arterially, or intranasally, depending on the availability and the severity of the situation. Oxybond can be especially useful in acute stroke centers, where rapid and effective intervention is crucial.

V. Experimental results of oxybond(Simulation)

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond has been tested in animal models of hemorrhagic shock and ischemic stroke, to evaluate its efficacy and safety as a synthetic blood substitute. The experimental results are summarized as follows:

- **Hemorrhagic shock:** Oxybond was administered to rats that were subjected to hemorrhagic shock, by withdrawing 40% of their blood volume, and then resuscitating them with either oxybond, blood, or saline, at a dose of 10 ml/kg. The survival rate, the blood pressure, the blood gas analysis, and the organ histology were measured and compared among the groups. The results showed that oxybond significantly improved the survival rate, the blood pressure, the oxygen delivery, and the organ function of the rats, compared to saline, and was comparable to blood. Oxybond also did not cause any hemolysis, coagulation, or inflammation, and was well tolerated by the rats. The results are shown in Table 1.

Treatment	Survival rate (%)	Blood pressure (mmHg)	Blood gas analysis	Organ histology
Oxybond	100	120/80	Normal	Normal
Blood	100	120/80	Normal	Normal
Saline	0	60/40	Hypoxic	Damaged

Table 1: Hemorrhagic shock

- Ischemic stroke: Oxybond was administered to mice that were subjected to ischemic stroke, by occluding the middle cerebral artery, and then reperfusing it after 60 minutes, with either oxybond, blood, or saline, at a dose of 5 ml/kg. The neurological score, the infarct volume, the brain edema, and the brain histology were measured and compared among the groups. The results showed that oxybond significantly reduced the neurological deficit, the infarct volume, the brain edema, and the brain damage of the mice, compared to saline, and was comparable to blood. Oxybond also did not cause any reperfusion injury, bleeding, or inflammation, and was well tolerated by the mice. The results are shown in Table 2.

Treatment	Neurological score	Infarct volume (mm3)	Brain edema (%)	Brain histology
Oxybond	0	10	5	Normal
Blood	0	10	5	Normal
Saline	4	50	10	Damaged

Table 2: Ischemic stroke

These experimental results demonstrate that oxybond is an effective and safe synthetic blood substitute, that can improve the outcome and the recovery of hemorrhagic shock and ischemic stroke, and that can be used as an alternative or an adjunct to blood transfusion.

VI. Discussion of oxybond

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond has been proposed as a novel synthetic blood substitute, that can overcome some of the limitations and risks of blood transfusion, and that can improve the outcome and the recovery of hemorrhagic shock and ischemic stroke. In this section, we discuss some of the advantages and challenges of using oxybond, as well as some of the future directions for research and development.

One of the main advantages of oxybond is its universal compatibility, which means that it can be administered to any patient, regardless of blood type, without the need for cross-matching and screening, and without the risk of immune reactions and transfusion errors. This can save time and

resources, and reduce the morbidity and mortality associated with blood transfusion. Oxybond can also be used in situations where blood supply and storage are limited or unavailable, such as remote areas, disaster zones, and war fields, where blood transfusion is often impractical or impossible. Oxybond can also be more acceptable than blood transfusion for some people, who may refuse to donate or receive blood for personal, cultural, or religious reasons, such as the Jehovah's Witnesses, who believe that blood transfusion violates the biblical commandment to abstain from blood.

Another advantage of oxybond is its infection-free nature, which means that it can be free of infectious agents, such as bacteria, viruses, parasites, and prions, that can cause serious diseases, such as hepatitis, HIV, malaria, and Creutzfeldt-Jakob disease. This can enhance the safety and quality of the product, and eliminate the risk of infection transmission. Oxybond can also be produced by chemical or biological synthesis, rather than derived from human or animal sources, which can avoid the ethical and regulatory issues associated with blood donation and transfusion, and respect the dignity and autonomy of the individuals involved.

A third advantage of oxybond is its long-term stability, which means that it can have a longer shelf life than donor blood, and that it can be stored at room temperature, without the need for refrigeration or special preservation methods. This can improve the stability and viability of the product, and facilitate its transportation and distribution. Oxybond can also have a longer circulation time than donor blood, as it does not undergo significant degradation or oxidation, unlike some HBOCs or PFCs, which can generate reactive oxygen species, free radicals, or toxic metabolites. This can reduce the dosage or frequency of administration, and minimize the potential harm and adverse reactions.

However, oxybond also has some challenges and limitations, that need to be addressed and resolved, before it can be widely used as a synthetic blood substitute. One of the main challenges is the optimization and regulation of its oxygen transport properties, such as its oxygen affinity, cooperativity, capacity, and solubility, which can affect its ability to deliver oxygen to the tissues, depending on the partial pressure of oxygen in the blood and the environment. Oxybond needs to have a balance between high and low oxygen affinity, to ensure adequate and efficient oxygen delivery to the tissues, without compromising the blood circulation and the tissue perfusion. Oxybond also needs to have a balance between high and low oxygen capacity and solubility, to ensure sufficient and uniform oxygen transport in the plasma, without causing problems of viscosity, rheology, and microcirculation. Oxybond also needs to have a mechanism to regulate its oxygen transport properties, in response to the physiological and pathological conditions, such as pH, temperature, carbon dioxide, nitric oxide, and other factors, that can modulate the oxygen demand and supply of the tissues. Oxybond also needs to be compatible with the endogenous components of blood, such as red blood cells, platelets, plasma proteins, and coagulation factors, and not interfere with their function and integrity.

Another challenge is the evaluation and testing of its biocompatibility and safety, such as its toxicity, side effects, metabolism, and excretion, which can affect its interaction with the biological components and systems of the body, and cause potential harm and adverse reactions. Oxybond needs to be non-toxic, non-immunogenic, non-inflammatory, non-vasoconstrictive, and non-hemolytic, and not cause oxidative stress, coagulation, or organ damage. Oxybond also needs to have a low metabolism, and be easily and rapidly excreted from the body, without accumulating or persisting in the tissues or organs. Oxybond also needs to be evaluated and tested in various animal models and clinical trials, to demonstrate its efficacy and superiority over blood transfusion, and to

determine its optimal dosage, concentration, route, and timing of administration, as well as its long-term effects and outcomes.

A third challenge is the development and production of oxybond, such as its synthesis, purification, characterization, and quality control, which can affect its availability and affordability as a synthetic blood substitute. Oxybond needs to have a simple and scalable synthesis, that can produce large quantities of oxybond, with high purity and quality, and low cost and waste. Oxybond also needs to have a reliable and standardized characterization, that can measure and verify its physical, chemical, and biological properties, such as its molecular weight, degree of polymerization, oxygen affinity, oxygen capacity, solubility, biocompatibility, and safety. Oxybond also needs to have a strict and consistent quality control, that can ensure the stability and viability of the product, and prevent the contamination or degradation of oxybond, during its storage and distribution.

These challenges and limitations of oxybond can be overcome by further research and development, such as:

- Designing and synthesizing new monomers and polymers, that can have different or tunable oxygen transport properties, such as oxygen affinity, cooperativity, capacity, and solubility, and that can respond to the physiological and pathological conditions, such as pH, temperature, carbon dioxide, nitric oxide, and other factors, that can modulate the oxygen demand and supply of the tissues.
- Developing and applying new methods and techniques, that can improve the synthesis, purification, characterization, and quality control of oxybond, such as microwave irradiation, nanotechnology, biotechnology, spectroscopy, chromatography, and calorimetry, that can increase the yield, purity, quality, and efficiency of oxybond, and reduce the cost, waste, and variability of oxybond.
- Conducting and expanding the evaluation and testing of oxybond, in various animal models and clinical trials, that can assess its efficacy and safety as a synthetic blood substitute, such as hemorrhagic shock, ischemic stroke, myocardial infarction, sepsis, and anemia, that can represent different scenarios and challenges of blood transfusion, and that can provide more data and evidence for the optimal use and regulation of oxybond.

In conclusion, oxybond is a promising synthetic blood substitute, that can overcome some of the limitations and risks of blood transfusion, and that can improve the outcome and the recovery of hemorrhagic shock and ischemic stroke. Oxybond has several advantages, such as universal compatibility, infection-free nature, and long-term stability, as well as some challenges, such as oxygen transport properties, biocompatibility and safety, and development and production, that need to be addressed and resolved, before it can be widely used as a synthetic blood substitute. Oxybond also has many potential applications, such as remote areas, disaster zones, and war fields, where blood transfusion is often impractical or impossible, as well as some ethical and religious issues, such as the respect for human dignity, the sanctity of life, and the autonomy of the donor and the recipient, that need to be considered and respected, when using oxybond as a synthetic blood substitute. Oxybond also has many future directions for research and development, such as designing and synthesizing new monomers and polymers, developing and applying new methods and techniques, and conducting and expanding the evaluation and testing of oxybond, that can improve the availability and affordability of oxybond, and enhance the therapeutic benefits of oxybond. Oxybond can be a revolutionary synthetic blood substitute, that can save lives and improve health, and that can be a valuable addition to the field of transfusion medicine

VII. Conclusion of oxybond

Oxybond is a synthetic polymer that can form reversible bonds with oxygen molecules, similar to hemoglobin. Oxybond has been proposed as a novel synthetic blood substitute, that can overcome some of the limitations and risks of blood transfusion, and that can improve the outcome and the recovery of hemorrhagic shock and ischemic stroke. In this paper, we have described the synthesis, properties, and applications of oxybond, and presented some experimental results that demonstrate its efficacy and safety in animal models of hemorrhagic shock and ischemic stroke. We have also discussed some of the advantages and challenges of using oxybond, as well as some of the future directions for research and development.

We have shown that oxybond has several advantages over blood transfusion, such as universal compatibility, infection-free nature, and long-term stability, which can save time and resources, and reduce the morbidity and mortality associated with blood transfusion. We have also shown that oxybond can be used in situations where blood supply and storage are limited or unavailable, such as remote areas, disaster zones, and war fields, where blood transfusion is often impractical or impossible. We have also shown that oxybond can be more acceptable than blood transfusion for some people, who may refuse to donate or receive blood for personal, cultural, or religious reasons, such as the Jehovah's Witnesses, who believe that blood transfusion violates the biblical commandment to abstain from blood.

We have also shown that oxybond has some challenges and limitations, that need to be addressed and resolved, before it can be widely used as a synthetic blood substitute. We have shown that oxybond needs to have a balance between high and low oxygen affinity, capacity, and solubility, to ensure adequate and efficient oxygen delivery to the tissues, without compromising the blood circulation and the tissue perfusion. We have also shown that oxybond needs to have a mechanism to regulate its oxygen transport properties, in response to the physiological and pathological conditions, such as pH, temperature, carbon dioxide, nitric oxide, and other factors, that can modulate the oxygen demand and supply of the tissues. We have also shown that oxybond needs to be compatible with the endogenous components of blood, such as red blood cells, platelets, plasma proteins, and coagulation factors, and not interfere with their function and integrity.

We have also shown that oxybond needs to be evaluated and tested in various animal models and clinical trials, to demonstrate its efficacy and superiority over blood transfusion, and to determine its optimal dosage, concentration, route, and timing of administration, as well as its long-term effects and outcomes. We have also shown that oxybond needs to be developed and produced by simple and scalable synthesis, reliable and standardized characterization, and strict and consistent quality control, to ensure the availability and affordability of oxybond, and to enhance the therapeutic benefits of oxybond.

We have concluded that oxybond is a promising synthetic blood substitute, that can overcome some of the limitations and risks of blood transfusion, and that can improve the outcome and the recovery of hemorrhagic shock and ischemic stroke. We have suggested that oxybond has many potential

applications, such as remote areas, disaster zones, and war fields, where blood transfusion is often impractical or impossible, as well as some ethical and religious issues, such as the respect for human dignity, the sanctity of life, and the autonomy of the donor and the recipient, that need to be considered and respected, when using oxybond as a synthetic blood substitute. We have also suggested that oxybond has many future directions for research and development, such as designing and synthesizing new monomers and polymers, developing and applying new methods and techniques, and conducting and expanding the evaluation and testing of oxybond, that can improve the availability and affordability of oxybond, and enhance the therapeutic benefits of oxybond. We have hoped that oxybond can be a revolutionary synthetic blood substitute, that can save lives and improve health, and that can be a valuable addition to the field of transfusion medicine.

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Appendix

The manufacturing process of oxybond can be divided into four steps: synthesis, purification, characterization, and quality control. The synthesis step involves the production of the monomer and the polymerization of the monomer. The purification step involves the isolation and the removal of the impurities and the by-products from the synthesis step. The characterization step involves the measurement and the verification of the physical, chemical, and biological properties of oxybond. The quality control step involves the testing and the validation of the stability and the viability of oxybond.

The synthesis step of oxybond can be performed by using a modified Schlenk reaction, which is a common method for preparing metal complexes with nitrogen ligands, and a condensation reaction, which is a common method for preparing polymers with covalent bonds. The synthesis step of oxybond can be carried out in a batch reactor, which is a type of reactor that operates in discrete cycles, rather than continuously. The batch reactor can be equipped with a heating system, a stirring system, a reflux system, a microwave system, and a sampling system, to control and monitor the reaction conditions and the reaction progress. The batch reactor can also be connected to a feed

tank, a product tank, a waste tank, and a solvent tank, to store and transfer the reactants, the products, the wastes, and the solvents.

The purification step of oxybond can be performed by using various methods and techniques, such as recrystallization, filtration, centrifugation, chromatography, and distillation, to isolate and remove the impurities and the by-products from the synthesis step. The purification step of oxybond can be carried out in a separation unit, which is a type of unit that separates the components of a mixture, based on their physical or chemical properties, such as solubility, polarity, size, shape, or boiling point. The separation unit can be equipped with a crystallizer, a filter, a centrifuge, a chromatograph, and a distiller, to perform the different methods and techniques of purification. The separation unit can also be connected to the product tank, the waste tank, and the solvent tank, to receive and send the products, the wastes, and the solvents.

The characterization step of oxybond can be performed by using various methods and techniques, such as spectroscopy, chromatography, calorimetry, and oxygen dissociation curve, to measure and verify the physical, chemical, and biological properties of oxybond, such as its molecular weight, degree of polymerization, oxygen affinity, oxygen capacity, solubility, biocompatibility, and safety. The characterization step of oxybond can be carried out in an analysis unit, which is a type of unit that analyzes the composition and the structure of a substance, based on its interaction with electromagnetic radiation, electric fields, magnetic fields, heat, or oxygen. The analysis unit can be equipped with a spectrometer, a chromatograph, a calorimeter, and an oxygen meter, to perform the different methods and techniques of characterization. The analysis unit can also be connected to the product tank, to receive and send the products.

The quality control step of oxybond can be performed by using various methods and techniques, such as stability test, viability test, sterility test, and toxicity test, to test and validate the stability and the viability of oxybond, and to prevent the contamination or the degradation of oxybond, during its storage and distribution. The quality control step of oxybond can be carried out in a testing unit, which is a type of unit that evaluates and verifies the quality and the performance of a product, based on its compliance with the specifications and the standards, such as the International Organization for Standardization (ISO), the Food and Drug Administration (FDA), and the European Medicines Agency (EMA). The testing unit can be equipped with a stability chamber, a viability chamber, a sterility chamber, and a toxicity chamber, to perform the different methods and techniques of quality control. The testing unit can also be connected to the product tank, to receive and send the products.