

NITRIC OXIDE SCAVENGERS

PRIORITY CLAIM

This application is a divisional of U.S. patent application Ser. No. 10/844,202, filed on May 12, 2004, the entire contents of which are incorporated herein by reference and relied upon.

BACKGROUND OF THE INVENTION

The present invention relates to therapeutic compositions. More specifically, the present invention relates to therapeutic compositions and methods of making and using same that are capable of removing excess nitric oxide effectively without inhibiting nitric oxide synthesis.

Due to disease, insult or other causes, a person's renal system can fail. In renal failure of any cause, there are several physiological derangements. The balance of water, minerals and the excretion of daily metabolic load are no longer possible in renal failure. During renal failure, toxic end products of nitrogen metabolism (e.g., urea, creatinine, uric acid, and the like) can accumulate in blood and tissues.

Kidney failure and reduced kidney function have been treated with dialysis. Dialysis removes waste, toxins and excess water from the body that would otherwise have been removed by normal functioning kidneys. Dialysis treatment for replacement of kidney functions is critical to many people because the treatment is life saving. One who has failed kidneys could not continue to live without replacing at least the filtration functions of the kidneys.

Hemodialysis, hemofiltration and peritoneal dialysis are three types of dialysis therapies generally used to treat loss of kidney function. Hemodialysis treatment removes waste, toxins and excess water directly from the patient's blood. The patient is connected to a hemodialysis machine, and the patient's blood is pumped through the machine. For example, needles or catheters can be inserted into the patient's veins and arteries to connect the blood flow to and from the hemodialysis machine. As blood passes through a dialyzer in the hemodialysis machine, the dialyzer removes the waste, toxins and excess water from the patient's blood and returns the blood to infuse back into the patient. A large amount of dialysate, for example about 90-120 liters, is used by most hemodialysis machines to dialyze the blood during a single hemodialysis therapy. The spent dialysate is then discarded. Hemodialysis treatment lasts several hours and is generally performed in a treatment center about three times per week.

Hemofiltration is a convection-based blood cleansing technique. Blood access can be venovenous or arteriovenous. As blood flows through the hemofilter, a transmembrane pressure gradient between the blood compartment and the ultrafiltrate compartment causes plasma water to be filtered across the highly permeable membrane. As the water crosses the membrane, it convects small and large molecules across the membrane and thus cleanses the blood. An excessive amount of plasma water is eliminated by filtration. Therefore, in order to keep the body water balanced, fluid must be substituted continuously by a balanced electrolyte solution (replacement or substitution fluid) infused intravenously. This substitution fluid can be infused either into the arterial blood line leading to the hemofilter (predilution) or into the venous blood line leaving the hemofilter.

Peritoneal dialysis utilizes a sterile dialysis solution or "dialysate", which is infused into a patient's peritoneal cavity and into contact with the patient's peritoneal mem-

brane. Waste, toxins and excess water pass from the patient's bloodstream through the peritoneal membrane and into the dialysate. The transfer of waste, toxins, and excess water from the bloodstream into the dialysate occurs due to diffusion and osmosis during a dwell period as an osmotic agent in the dialysate creates an osmotic gradient across the membrane. The spent dialysate is later drained from the patient's peritoneal cavity to remove the waste, toxins and excess water from the patient.

There are various types of peritoneal dialysis therapies, including continuous ambulatory peritoneal dialysis ("CAPD") and automated peritoneal dialysis. CAPD is a manual dialysis treatment, in which the patient connects the catheter to a bag of fresh dialysate and manually infuses fresh dialysate through the catheter or other suitable access device and into the patient's peritoneal cavity. The patient disconnects the catheter from the fresh dialysate bag and allows the dialysate to dwell within the cavity to transfer waste, toxins and excess water from the patient's bloodstream to the dialysate solution. After a dwell period, the patient drains the spent dialysate and then repeats the manual dialysis procedure. Tubing sets with "Y" connectors for the solution and drain bags are available that can reduce the number of connections the patient must make. The tubing sets can include pre-attached bags including, for example, an empty bag and a bag filled with dialysate.

In CAPD, the patient performs several drain, fill, and dwell cycles during the day, for example, about four times per day. Each treatment cycle, which includes a drain, fill and dwell, takes about four hours.

Automated peritoneal dialysis is similar to continuous ambulatory peritoneal dialysis in that the dialysis treatment includes a drain, fill, and dwell cycle. However, a dialysis machine automatically performs three or more cycles of peritoneal dialysis treatment, typically overnight while the patient sleeps.

With automated peritoneal dialysis, an automated dialysis machine fluidly connects to an implanted catheter. The automated dialysis machine also fluidly connects to a source or bag of fresh dialysate and to a fluid drain. The dialysis machine pumps spent dialysate from the peritoneal cavity, through the catheter, to the drain. The dialysis machine then pumps fresh dialysate from the dialysate source, through the catheter, and into the patient's peritoneal cavity. The automated machine allows the dialysate to dwell within the cavity so that the transfer of waste, toxins and excess water from the patient's bloodstream to the dialysate solution can take place. A computer controls the automated dialysis machine so that the dialysis treatment occurs automatically when the patient is connected to the dialysis machine, for example, when the patient sleeps. That is, the dialysis system automatically and sequentially pumps fluid into the peritoneal cavity, allows for dwell, pumps fluid out of the peritoneal cavity, and repeats the procedure.

Several drain, fill, and dwell cycles will occur during the treatment. Also, a smaller volume "last fill" is typically used at the end of the automated dialysis treatment, which remains in the peritoneal cavity of the patient when the patient disconnects from the dialysis machine for the day. Automated peritoneal dialysis frees the patient from having to manually perform the drain, dwell, and fill steps during the day.

In general, standard peritoneal dialysis solutions contain dextrose or other suitable osmotic agent at a suitable concentration, such as 1.5% to 4.25% by weight, to effect transport of water and metabolic waste products across the