Pharmaceutical Composition for Preventing or Treating Diabetic Nephropathy

【Technical Field】

The present invention relates to a pharmaceutical composition for prevention or treatment of diabetic nephropathy, which contains fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof. More specifically, the present invention relates to a pharmaceutical composition capable of preventing diabetic nephropathy or inhibiting the progression of diabetic nephropathy and effectively alleviating various symptoms caused by diabetic nephropathy.

【Background Art】

Diabetes is a type of metabolic disease in which insulin secretion is deficient or dysfunctional. It is characterized by hyperglycemia in which blood sugar levels are elevated. Due to hyperglycemia, various symptoms and signs occur, and glucose is excreted in the urine.

When a diabetic patient suffers from hyperglycemia over a long period of time, other chronic complications may occur, including peripheral neuropathy, autonomic neuropathy, macrovascular complications, and microvascular complications.

Diabetic nephropathy is one of complications caused by diabetes. It is the most important cause of chronic renal failure, and accounts for a large proportion of the underlying diseases of all dialysis patients.

Diabetic nephropathy is usually asymptomatic at the initial stage, and there is no obvious symptom other than proteinuria appearing in a urine test as it progresses. Therefore, the onset of diabetic nephropathy is diagnosed by the finding of microalbuminuria (urine albumin secretion: 30-299 mg / 24 h).

However, since the microalbuminuria symptom as described above is also found after diabetic nephropathy progresses considerably, diabetic nephropathy is not easy to diagnose early and is found after considerable progression in most cases.

In the case of diabetic nephropathy, intervascular tissue becomes hypertrophic due to abnormal proliferation of mesangial cells, resulting in thickening of the glomerular basement membrane and the tubular basement membrane and narrowing of the inner diameter of glomerular vessels.

As glomerular mesangial areas increase and extracellular lipid accumulation, glomerular sclerosis and tubulointerstitial fibrosis progress, the function of the kidney gradually becomes weaker, ultimately leading to chronic renal failure.

Another clinical significance of diabetic nephropathy is a significant increase in mortality. The mortality rate of type 1 diabetic patients with marked proteinuria is significantly higher than those of type 1 diabetic patients with normal albuminuria and normal people. That is, among diabetic patients, the mortality rate of patients with

diabetes-induced kidney disease significantly increases.

The proportion of such diabetic nephropathy in kidney diseases is gradually increasing as the number of diabetic patients is increasing. Especially, the number of patients with type 2 kidney disease is continuously increasing.

However, to date, there are little or no drugs having a preventive or therapeutic effect against diabetic nephropathy. Furthermore, when drugs that have been used in the past are used over a long period of time, they can cause many side effects, such as hyperkalemia, and even acute renal failure due to functional or organic renal artery stenosis.

Therefore, it is very important to develop a new drug for safe and effective prevention and treatment of diabetic nephropathy.

[Prior Art Documents]

[Patent Documents]

Korean Patent No. 0354654

[Non-Patent Document]

Cardiovasc Diabetol. 2009 Jan 21; 8:4, Gurney AM;

Metabolism. 1979 Nov; 28(11):1075-7, Somani P et al.

【Disclosure】

【Technical Problem】

It is an object of the present invention to provide a pharmaceutical composition for prevention or treatment of diabetic nephropathy, which contains fimasartan, a

pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

Another object of the present invention is to provide the use of fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, for prevention or treatment of diabetic nephropathy.

Still another object of the present invention is to provide a method of preventing or treating diabetic nephropathy by administering to a subject a pharmaceutical composition containing fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

【Technical Solution】

The present invention provides a pharmaceutical composition for prevention or treatment of diabetic nephropathy, which contains fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

In the present invention, the diabetic nephropathy refers to a kidney disorder that occurs in a patient suffering from diabetes, and is a typical complication caused by diabetes. This disease is caused by diabetes-induced hyperglycemia, which results in damage to glomeruli in the kidneys and deterioration of kidney function.

Diabetic nephropathy shows no particular symptoms other than the detection of microalbuminuria in urine, and thus treatment thereof tends to be delayed, resulting in chronic

renal failure, which leads to a state in which kidney transplantation is necessary or to death.

Therefore, in the case of diabetic nephropathy, it is important to prevent diabetic nephropathy from occurring in a subject with diabetes or to delay the occurrence of diabetic nephropathy as much as possible. In addition, when diabetic nephropathy occurred, it is important to alleviate the symptoms thereof or prevent the symptoms from worsening, thereby inhibiting the progression of the diabetic nephropathy or slowing the progression rate of the disease.

The pharmaceutical composition containing fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, can effectively prevent or treat diabetes-induced kidney disease. As a result, it can prevent, or inhibit or delay the onset of kidney disease in a subject suffering from diabetes, or can ameliorate the symptoms of diabetic kidney disease in a subject with diabetic nephropathy, and inhibit the progression of kidney disease or slow the progression rate of the disease, thereby preventing the disease from worsening.

Therefore, the composition according to the present invention can prevent diabetic nephropathy from leading to chronic renal failure, thereby significantly reducing the mortality rate of the subjects. Furthermore, when diabetic nephropathy leads to chronic renal failure, it eventually leads

to dialysis. In connection with this, the pharmaceutical composition containing fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, can inhibit or delay the progression of diabetic nephropathy, thereby delaying the initiation of the above-described dialysis.

In the present invention, the prevention refers to all actions that prevent, inhibit or delay the onset of diabetic nephropathy or symptoms thereof by administering the pharmaceutical composition according to the present invention. For example, when the composition of the present invention is administered to a subject who has developed diabetes but has yet not developed diabetic nephropathy, it can prevent or delay the occurrence of diabetic nephropathy or symptoms thereof.

In the present invention, the treatment refers to all actions that alleviate or beneficially change diabetic nephropathy or symptoms thereof or inhibit or delay of diabetic nephropathy and thereby prevent diabetic nephropathy from worsening, by administering the pharmaceutical composition according to the present invention. For example, when the composition of the present invention is administered to a subject who has developed diabetic nephropathy, it can alleviate or beneficially change diabetic nephropathy or symptoms thereof. Alternatively, when the composition of the present invention is administered to a subject who has developed diabetic nephropathy, it can inhibit or delay the

progression of diabetic nephropathy or symptoms thereof, thereby preventing diabetic nephropathy from worsening. As a result, it can prevent diabetic nephropathy from leading chronic renal failure, thereby significantly reducing the mortality caused by diabetic nephropathy and delaying the start of dialysis.

In the present invention, the treatment comprises reducing the mortality caused by diabetic nephropathy and delaying the start of dialysis.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent the occurrence of albuminuria or proteinuria, or reduce the amount of albuminuria or proteinuria, or inhibit an increase in the amount.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent serum creatinine and blood urea nitrogen levels from increasing, or reduce the levels, or inhibit an increase in the levels.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent nephron damage, glomerular sclerosis and fibrosis, intraglomerular basement membrane thickening, vacuolar degeneration and necrosis, tubular basement membrane thickening, tubular damage,

tubulointerstitial fibrosis, hydronephrosis, and an increase in kidney volume, or ameliorate the above-described symptoms, or inhibit the symptoms, or delaying the progression of the symptoms, thereby preventing the symptoms from worsening.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent the occurrence of local inflammation of kidney cells, or alleviate inflammation of kidney cells, or inhibit the inflammation or delay the progression of the inflammation, thereby preventing the inflammation from worsening.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent protein accumulation in tubular lumens, or alleviating a symptom of protein accumulation in tubular lumens, or delay protein accumulation in tubular lumens.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent an increase in mesangial cells or the accumulation of extracellular matrix protein, or alleviate, inhibit or delay these symptoms.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can prevent the occurrence of edema,

itching and uremic symptoms caused by kidney disease, or reduce the edema, itching and uremic symptoms, or delay the worsening of the edema, itching and uremic symptoms.

When the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy, it can reduce and alleviate the anorexia and fatigue caused by kidney disease, and delay the worsening of the anorexia and fatigue caused by kidney disease.

When the composition of the present invention is administered to a subject with diabetic nephropathy, it can prevent the progression of diabetic nephropathy or reduce the rate of progression of diabetic nephropathy, thereby preventing or delaying chronic renal failure, which may result in significantly lowering the mortality of the subject or delaying the start of dialysis.

The composition of the present invention can sufficiently effectively prevent or treat diabetic nephropathy, even when it contains, as an active ingredient, only fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

The composition of the present invention exhibits sufficient safety so that it may be administered to a subject for a long period of time. For example, even when the composition of the present invention is administered to a subject with diabetes or a subject with diabetic nephropathy,

it does not cause hyperkalemia and the irregular heartbeat or cardiac arrest resulting from hyperkalemia, and does not cause kidney disorders such as acute renal failure due to functional or organic renal artery stenosis, and has little or no toxicity including other side effects.

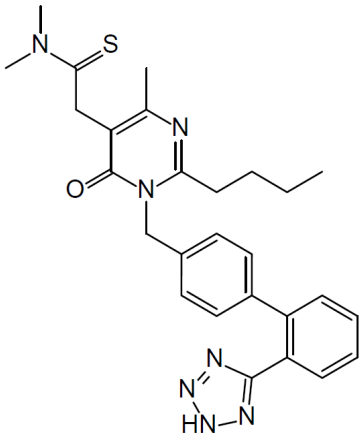
Therefore, the fimasartan, pharmaceutically acceptable salt thereof or hydrate or solvate thereof according to the present invention may also be administered safely to subjects with diabetes or diabetic nephropathy for a long period of time.

In the present invention, the subjects refer to animals including humans. For example, the subjects may be mammals, including mice, rats, other rodents, rabbits, dogs, pigs, cats, cattle, sheep, horses, primates, and humans. Preferably, the subjects may be primates, more preferably humans.

In the present invention, the diabetes may be insulin-dependent type 1 diabetes or non-insulin-dependent type 2 diabetes.

In the present invention, the fimasartan may be a compound represented by Formula 1 below:

[Formula 1]



In the present invention, the pharmaceutically acceptable salt refers to an inorganic acid salt, an organic acid salt or a metal salt, which is generally used by pharmaceutical manufacturers to manufacture pharmaceuticals. An organic acid that may be used is hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid or the like; an organic acid that may be used is citric acid, acetic acid, lactic acid, tartaric acid, fumaric acid, formic acid, propionic acid, oxalic acid, trifluoroacetic acid, methanesulfonic acid, benzenesulfonic acid, maleic acid, benzoic acid, gluconic acid, glycolic acid, succinic acid, 4-morpholineethanesulfonic acid, camphorsulfonic acid, 4-nitrobenzenesulfonic acid, hydroxy-O-sulfonic acid, 4-toluenesulfonic acid, galacturonic acid, embonic acid, glutamic acid, aspartic acid, adipic acid, camsyl acid or the like; and a metal that may be used is sodium,

potassium, calcium, magnesium or the like.

In the present invention, the salt of fimasartan may preferably be fimasartan potassium salt, hydrochloride, calcium salt, sulfate, adipate, camsylate or besylate. More preferably, it may be fimasartan potassium salt. These salts may be commercially available or may be prepared according to a known method (for example, Korean Patent No. 0354654).

In the present invention, the hydrate may include a stoichiometric or nonstoichiometric amount of water bound by non-covalent intermolecular forces.

In the present invention, the solvate may include a stoichiometric or nonstoichiometric amount of a solvent bound by non-covalent intermolecular forces. The solvent refers to a conventional solvent which is used for preparation of organic compounds, and examples thereof include methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, 1-acetate, acetone, acetic acid, anisole, tetrahydrofuran, methyl acetate, ethyl acetate, propyl acetate, isopropyl acetate, isobutyl acetate, n-butyl acetate, dimethyl sulfoxide, pentane, heptane, and the like, but the solvate of the present invention is not limited by these examples.

In the present invention, the hydrate and the solvate may contain water or a solvent in an amount of 0.25 to 10 moles, for example, 0.5 moles, 1 mole, 1.5 moles, 2 moles, 2.5 moles, 3 moles, 5 moles and the like, per mole of fimasartan potassium.

Preferably, these may contain water in an amount of 1 mole or 3 moles per mole of fimasartan potassium. For example, the pharmaceutical composition may be prepared using fimasartan potassium salt monohydrate or fimasartan potassium salt trihydrate.

In the present invention, the pharmaceutical composition may contain fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, in an amount of 5 wt% to 60 wt%, preferably 10 wt% to 50 wt%, based on the total weight of the composition.

In the present invention, the pharmaceutical composition may further contain pharmaceutically acceptable additives. The term "pharmaceutically acceptable" relates to substances which are physiologically tolerable and normally do not cause an allergic reaction or similar adverse reaction, such as gastric discomfort, dizziness and the like, when they are administered to a human being, and which are generally used by those skilled in the art to prepare pharmaceutical compositions. For these substances, reference may be made to Remington's Pharmaceutical Science (the latest edition), Mack Publishing Company, Easton PA.

The additives may include carriers, excipients, extenders, antioxidants, buffers, fillers, antiadherents, lubricants, wetting agents, flavoring agents, emulsifiers, suspending agents, surfactants, preservatives, and the like. For example,

the additives include lactose, dextrose, calcium silicate, corn starch, sucrose, sorbitol, mannitol, xylitol, erythritol, maltitol, starch, acacia rubber, alginate, gelatin, calcium phosphate, calcium silicate, cellulose, methyl cellulose, polyvinylpyrrolidone, water, methyl hydroxybenzoate, propyl hydroxybenzoate, talc, stearic acid, magnesium stearate, calcium stearate, mineral oil, saline solution, glucose solution, sugar-like solution, alcohol, glycol, ether (e.g. polyethyleneglycol 400), oil, fatty acid, fatty acid ester, glyceride, or mixtures thereof. However, additives that may be contained in the composition according to the present invention are not limited to the above-listed substances which are only illustrative.

The pharmaceutical composition of the present invention may be formulated according to a conventional method, and may be prepared as a formulation for oral administration or a formulation for parenteral administration. Preferably, it may be prepared as a formulation for oral administration.

In the present invention, the formulation for oral administration may be a solid formulation such as a tablet, pill, powder, granule or capsule formulation, or may be a liquid formulation such as a suspension, solution, emulsion or syrup formulation. It may preferably be a solid formulation, more preferably a tablet formulation.

When the pharmaceutical composition of the present

invention is prepared as an oral solid formulation, examples of additives that may be used include cellulose, calcium silicate, corn starch, lactose, sucrose, dextrose, calcium phosphate, stearic acid, magnesium stearate, calcium stearate, gelatin, talc, and the like.

When the pharmaceutical composition of the present invention is prepared as a liquid formulation for oral administration, the pharmaceutical composition may be formulated using various additives, including simple diluents, such as water or liquid paraffin, wetting agents, sweetening agents, flavoring agents, preservatives, coloring agents, and the like.

When the pharmaceutical composition of the present invention is prepared as an injectable formulation, additives may be used, including water, saline, aqueous glucose solution, aqueous sugar-like solution, alcohol, glycol, ether (e.g., polyethyleneglycol 400), oil, fatty acid, fatty acid ester, glyceride, and the like.

In the present invention, the contents of additives in the pharmaceutical composition are not particularly limited, and may be suitably adjusted within the content ranges which are used in conventional formulation.

In the present invention, the pharmaceutical composition may contain fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof such that the content

of fimasartan is 1 mg to 240 mg, preferably about 30 to 180 mg.

In the present invention, the pharmaceutical composition may be administered orally or parenterally (e.g., intravenously, subcutaneously, intraperitoneally or locally), and the dose thereof may vary depending on the patient's weight, age, sex, health condition, diet, the time of administration, the mode of administration, the duration or interval of administration, excretion rate, constitutional specificity, the properties of the formulation, the severity of the disease, and the like. For example, for an adult weighing about 60 kg, fimasartan may be administered orally once or several times daily at a dose of about 1 to 240 mg/day, preferably 30 to 180 mg/day.

In the present invention, the pharmaceutical composition may further contain, in addition to fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, other active ingredient having pharmacological activity.

The pharmaceutical composition of the present invention may further contain, in addition to fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, an antihypertensive agent, a diuretic, a hyperlipidemia-treating agent, an anti-obesity agent or a diabetes-treating agent. For example, in addition to fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof as an active ingredient, the

composition of the present invention may further contain amlodipine, nifedipine, verapamil, diltiazem, nicardipine, lercardipine, atorvastatin, cerivastatin, fluvastatin, lovastatin, pitavastatin, simvastatin, rosuvastatin, nicotinic acid, theophylline, caffeine, theobromine, aminophylline, hydrochlorothiazide, bendroflumethiazide, alogliptin, saxagliptin, sitagliptin, metformin, exenatide, rosiglitazone, pioglitazone, tolbutamide, troglitazone, leptin, ephedrine, fenfluramine, fluoxetine, or the like.

For the improvement, alleviation, treatment or prevention of diabetic nephropathy, the pharmaceutical composition of the present invention may be used alone or in combination with surgery, hormonal therapy, drug therapy, and methods employing biological response regulators.

The present invention provides the use of fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, for the prevention or treatment of diabetic nephropathy.

The present invention provides a method of preventing or treating diabetic nephropathy by administering to a subject a pharmaceutical composition containing fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

In the use and method of the present invention, the pharmaceutical composition and fimasartan, a pharmaceutically

acceptable salt thereof, or a hydrate or solvate thereof, which is contained in the composition, are as described above.

【Advantageous Effects】

The pharmaceutical composition according to the present invention, which contains fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, can effectively prevent or treat diabetic nephropathy. The pharmaceutical composition according to the present invention can prevent or inhibit the onset of diabetic nephropathy, and can also alleviate diabetic nephropathy, or inhibit the progression or worsening of diabetic nephropathy.

【Description of Drawings】

FIGS. 1 and 2 show the reduction in urine albumin excretion in rats by administration of the pharmaceutical composition of the present invention.

【Mode for Invention】

Hereinafter, the present invention will be described in detail with reference to examples in order to help understand the present invention. However, these examples are only to illustrate the present invention, and the scope of the present invention is not limited to these examples. These examples of the present invention are provided to more fully explain the present invention to those skilled in the art. The experimental results of each example were statistically processed using ANOVA (one way analysis of variance). When

significance was acknowledged, significance was tested using Dunnett's multiple comparison test at p <0.05 (* or †) or p <0.01 (**).

1. Preparation of Experimental Animals

(1) Selection of Experimental Animals

8-Week-old spontaneously hypertensive rats (SHRs; weighed 245 to 260 g) were purchased and housed for 2 weeks at a temperature of 22±3°C, a humidity of 55±15%, 10 to 20 ventilations/hr, a 12-hr light/12-hr dark cycle (light at 8am and then dark at 8pm) and an illuminance of 150 to 300 Lux. During the housing period, the rats were allowed to access experimental animal food (produced by Cargill Agri Purina, Inc. and supplied from Dreambio, Co., Ltd.) *ad libitum*. In addition, the rats were allowed to access water (purified water contained in a drinking water bottle made of polycarbonate) *ad libitum*. Next, for use in an experiment, 19 healthy rats were selected and grouped into group 1 (6 rats), group 2 (6 rats) and group 3 (7 rats).

(2) Induction of Diabetic Nephropathy

Streptozotocin (STZ) was used to induce diabetic nephropathy in the rats (Gurney AM, Cardiovasc Diabetol. 2009 Jan 21;8:4; Somani P et al., Metabolism. 1979 Nov;28(11):1075-7). When streptozotocin is administered intraperitoneally or intravenously, it induces a diabetic condition by destroying pancreatic beta-cells.

Streptozotocin was administered to group 2 and group 3. One day before administration of streptozotocin, the rats were fasted for one day by fasting plates. A composition containing streptozotocin dissolved in 0.1M sodium citrate buffer (pH 4.5) was administered to the fasted rats at a dose of 1 mL/kg such that the content of streptozotocin in each rat would be 50 mg/kg immediately after fasting blood glucose measurement. After 48 hours from administration of streptozotocin, fasting blood glucose levels were measured. When the measured blood glucose levels were 250 mg/dl or higher, it was determined that diabetes was induced. The diabetes-induced rats were used in an experiment.

2. Administration of Drugs

After 48 hours from administration of streptozotocin, induction of diabetes was confirmed, and drugs were administered.

To the rats of group 3, a solution prepared by dissolving fimasartan potassium salt trihydrate in a 0.5% (v/v) aqueous solution of carboxymethyl cellulose (SAMCHUN PURE CHEMICAL CO., LTD.) was administered once daily for 24 weeks at a dose of 4 mL/kg such that the content of fimasartan would be 10 mg/Kg/day.

To group 1 and group 2, 0.5% (v/v) carboxymethyl cellulose (SAMCHUN PURE CHEMICAL CO., LTD.) was administered at a dose of 4 mL/Kg/day.

To each group, carboxymethyl cellulose aqueous solution

and fimasartan were administered orally once a day before 4pm. For oral administration, the animals were fixed by a dorsal skin fixing method, and the drug was administered directly into the stomach by an oral zonde.

<Example 1> Evaluation 1 of Preventive and Therapeutic Effects of Fimasartan against Diabetic Nephropathy

Each rat group administered with carboxymethyl cellulose aqueous solution or fimasartan for 24 weeks was subjected to a urine test at 2-week intervals. The rats of each group were placed in metabolic cages, and urine was collected therefrom for 24 hours, after which urine creatinine excretion (CRE) and urine albumin excretion (UAE) were measured using a blood biochemical analyzer (7020 Hitachi, Japan). The results of measurement of the urine albumin excretion (UAE) are shown in FIG. 1, and the results of measurement of urine albumin-to-urine creatinine ratio (UACR) are shown in FIG. 2.

As can be seen in FIGS. 1 and 2, urine albumin excretion in group 2 and group 3 administered with streptozotocin increased compared to that in group 1 not administered with streptozotocin, suggesting that diabetic nephropathy occurred in groups 2 and 3. However, it could be seen that urine albumin excretion in group 3 administered with fimasartan significantly decreased compared to that in group 2 with streptozotocin-induced diabetes.

In general, the most common symptom of diabetic

nephropathy is the detection of albumin in urine. When fimasartan was administered to the subjects with diabetic nephropathy, it reduced urine albumin excretion in the subjects, suggesting that fimasartan can prevent or significantly alleviate diabetic nephropathy.

<Example 2> Evaluation 2 of Preventive and Therapeutic Effects of Fimasartan against Diabetic Nephropathy

After the drugs were administered to group 1 to group 3 for 24 weeks, the rats of each group were subjected to histopathology.

For histopathology, left kidney tissue and right kidney tissue were separately prepared as sample tissues. The right kidney tissue was trimmed perpendicular to the long axis, and the left kidney tissue was trimmed parallel to the long axis. Each trimmed sample tissue was fixed in 10% neutral formalin solution for 24 hours, and then cut to a thickness of 3 mm. The sample tissue cut to a thickness of 3 mm was embedded in paraffin, and sectioned using a microtome, thereby preparing 4-μm tissue sections. The sections were stained with Hematoxylin & Eosin (H&E), and then subjected to histopathology using an optical microscope (Olympus, BX41, Japan).

6 tissue samples from group 1, 8 tissue samples from group 2, and 8 tissue samples from group 3 were obtained, and then subjected to histopathology, and the degree of tubular vacuolar degeneration and necrosis was analyzed.

For histopathological evaluation, the extent of lesions was scored as follows: (0) none; (1) smallest; (2) less; (3) moderate; and (4) distinct. The results are shown in Tables 1 to 3 below.

Table 1: Group 1

Histopathology	1R	1L	2R	2L	3R	3L	Mean
Vacuolar degeneration/necrosis	0	0	0	0	0	0	0.0±0.00

(R: right kidney, L: left kidney)

Table 2: Group 2

Histopathology	1R	1L	2R	2L	3R	3L	4R	4L	Mean
Vacuolar degeneration/necrosis	2	1	2	1	2	2	3	3	2.0±0.76

(R: right kidney, L: left kidney)

Table 3: Group 3

Histopathology	1R	1L	2R	2L	3R	3L	4R	4L	Mean
Vacuolar degeneration/necrosis	2	1	0	0	1	1	1	1	0.9±0.64

(R: right kidney, L: left kidney)

As can be seen in Tables 1 to 3 above, when comparing

group 2 and group 3, each administered with streptozotocin (STZ), lesions such as tubular vacuolar degeneration in group 3 administered with fimasartan significantly decreased compared to those in group 2.

This suggests that fimasartan can significantly reduce the extent of kidney cell lesions caused by diabetic nephropathy and that fimasartan can significantly alleviate diabetic nephropathy and delay the progression of diabetic nephropathy.

【Industrial Applicability】

The pharmaceutical composition according to the present invention contains fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof, and can effectively prevent or treat diabetic nephropathy. The pharmaceutical composition according to the present invention can prevent or inhibit the onset of diabetic nephropathy, and can also alleviate diabetic nephropathy, or inhibit the progression or worsening of diabetic nephropathy.

CLAIMS

1. A pharmaceutical composition for preventing or treating diabetic nephropathy comprising fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutically acceptable salt is a fimasartan potassium salt.

3. The pharmaceutical composition of claim 1, wherein the hydrate is a fimasartan potassium salt trihydrate.

4. The pharmaceutical composition of claim 1, wherein the composition further contains pharmaceutically acceptable additives.

5. The pharmaceutical composition of claim 1, wherein the composition is for oral administration.

6. The pharmaceutical composition of claim 1, wherein the composition contains, based on the total weight of the composition, 5 wt% to 60 wt% of fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.

7. A method of preventing or treating diabetic nephropathy by administering to a subject a pharmaceutical composition comprising fimasartan, a pharmaceutically acceptable salt thereof, or a hydrate or solvate thereof.