[0018] Through repeated experiments, the Applicant has found that the above-mentioned form of penehyclidine hydrochloride has a good effect in the treatment and/or prevention of diseases such as myopia and amblyopia.

[0019] According to an embodiment of the present disclosure, the medicament is for use in the treatment and/or prevention of myopia and/or amblyopia.

[0020] According to an embodiment of the present disclosure, the myopia and/or amblyopia includes one or more of mild myopia, moderate myopia, high myopia, axial myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, fundus damage, visual distortion, double vision, abnormal color vision, abnormal light vision, decreased contrast sensitivity, and ametropic amblyopia. It should be noted that the vision-impairing eye diseases described herein do not include vision problems caused by trauma.

[0021] In a second aspect of the present disclosure, the present disclosure provides a pharmaceutical composition for treating and/or preventing vision-impairing eye diseases. According to an embodiment of the present disclosure, the composition includes, as an active ingredient, the compound having the structure represented by Formula (I), or the nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug thereof.

[0022] According to an embodiment of the present disclosure, the above-mentioned pharmaceutical composition may further include at least one of the following additional technical features:

[0023] According to an embodiment of the present disclosure, the pharmaceutical composition is for use in the treatment and/or prevention of myopia and/or amblyopia.

[0024] According to an embodiment of the present disclosure, the myopia and/or amblyopia includes one or more of mild myopia, moderate myopia, high myopia, axial myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, fundus damage, visual distortion, double vision, abnormal color vision, abnormal light vision, decreased contrast sensitivity, and ametropic amblyopia. It should be noted that the vision-impairing eye diseases described herein do not include vision problems caused by trauma.

[0025] According to an embodiment of the present disclosure, the pharmaceutical composition further includes at least one pharmaceutically acceptable carrier. In the pharmaceutical composition according to the embodiments of the present disclosure, the

carriers include, but are not limited to, aqueous solvents, water-miscible solvents, non-aqueous solvents, antimicrobial agents or preservatives against the growth of microorganisms, stabilizers, solubility enhancers, osmotic pressure regulators, buffers, antioxidants, local anesthetics, suspending and dispersing agents, wetting or emulsifying agents, complexing agents, sequestering or chelating agents, antifreeze agents, cryoprotectants, thickening agents, pH-adjusting agents, and inert gases, which can be selected by those skilled in the art according to the actual requirements of the formulation.

[0026] According to an embodiment of the present disclosure, the pharmaceutical composition is in in a formulation of an ophthalmic preparation, and the ophthalmic preparation includes one or more of eye drops, eye ointment, eye cream, eye emulsion, eye gel, eye pill, eye membrane, or intraocular implant.

[0027] According to an embodiment of the present disclosure, a mass fraction of the active ingredient in the pharmaceutical composition ranges from 0.005% to 2%, based on a mass of the pharmaceutical composition. In the pharmaceutical composition according to the embodiments of the present disclosure, the mass fraction of the active ingredient in the pharmaceutical composition is 0.005%, 0.01%, 0.015%, 0.02%, 0.025%, 0.03%, 0.035%, 0.04%, 0.045%, 0.05%, 0.055%, 0.06%, 0.065%, 0.07%, 0.075%, 0.08%, 0.085%, 0.09%, 0.095%, 0.1%, 0.105%, 0.11%, 0.115%, 0.12%, 0.125%, 0.13%, 0.135%, 0.14%, 0.145%, 0.15%, 0.155%, 0.16%, 0.165%, 0.17%, 0.175%, 0.18%, 0.185%, 0.19%, 0.195%, 0.2%, 0.205%, 0.21%, 0.215%, 0.22%, 0.225%, 0.23%, 0.235%, 0.24%, 0.245%, 0.25%, 0.255%, 0.26%, 0.265%, 0.27%, 0.275%, 0.28%, 0.285%, 0.29%, 0.295%, 0.3%, 0.305%, 0.31%, 0.315%, 0.32%, 0.325%, 0.33%, 0.335%, 0.34%, 0.345%, 0.35%, 0.355%, 0.36%, 0.365%, 0.37%, 0.375%, 0.38%, 0.385%, 0.39%, 0.395%, 0.4%, 0.405%, 0.41%, 0.415%, 0.42%, 0.425%, 0.43%, 0.435%, 0.44%, 0.445%, 0.45%, 0.455%, 0.46%, 0.465%, 0.47%, 0.475%, 0.48%, 0.485%, 0.49%, 0.495%, 0.5%, 0.505%, 0.510%, 0.515%, 0.520%, 0.525%, 0.530%, 0.535%, 0.540%, 0.545%, 0.550%, 0.555%, 0.560%, 0.565%, 0.570%, 0.575%, 0.580%, 0.585%, 0.590%, 0.595%, 0.600%, 0.605%, 0.610%, 0.615%, 0.620%, 0.625%, 0.630%, 0.635%, 0.640%, 0.645%, 0.650%, 0.655%, 0.660%, 0.665%, 0.670%, 0.675%, 0.680%, 0.685%, 0.690%, 0.695%, 0.700%, 0.705%, 0.710%, 0.715%, 0.720%, 0.725%, 0.730%, 0.735%, 0.740%, 0.745%, 0.750%, 0.755%, 0.760%, 0.765%, 0.770%, 0.775%, 0.780%,

0.785%, 0.790%, 0.795%, 0.800%, 0.805%, 0.810%, 0.815%, 0.820%, 0.825%, 0.830%, 0.835%, 0.840%, 0.845%, 0.850%, 0.855%, 0.860%, 0.865%, 0.870%, 0.875%, 0.880%, 0.885%, 0.890%, 0.895%, 0.900%, 0.905%, 0.910%, 0.915%, 0.920%, 0.925%, 0.930%, 0.935%, 0.940%, 0.945%, 0.950%, 0.955%, 0.960%, 0.965%, 0.970%, 0.975%, 0.980%, 0.985%, 0.990%, 0.995%, 1.000%, 1.005%, 1.010%, 1.015%, 1.020%, 1.025%, 1.030%, 1.035%, 1.040%, 1.045%, 1.050%, 1.055%, 1.060%, 1.065%, 1.070%, 1.075%, 1.080%, 1.085%, 1.090%, 1.095%, 1.100%, 1.105%, 1.110%, 1.115%, 1.120%, 1.125%, 1.130%, 1.135%, 1.140%, 1.145%, 1.150%, 1.155%, 1.160%, 1.165%, 1.170%, 1.175%, 1.180%, 1.185%, 1.190%, 1.195%, 1.200%, 1.205%, 1.210%, 1.215%, 1.220%, 1.225%, 1.230%, 1.235%, 1.240%, 1.245%, 1.250%, 1.255%, 1.260%, 1.265%, 1.270%, 1.275%, 1.280%, 1.285%, 1.290%, 1.295%, 1.300%, 1.305%, 1.310%, 1.315%, 1.320%, 1.325%, 1.330%, 1.335%, 1.340%, 1.345%, 1.350%, 1.355%, 1.360%, 1.365%, 1.370%, 1.375%, 1.380%, 1.385%, 1.390%, 1.395%, 1.400%, 1.405%, 1.410%, 1.415%, 1.420%, 1.425%, 1.430%, 1.435%, 1.440%, 1.445%, 1.450%, 1.455%, 1.460%, 1.465%, 1.470%, 1.475%, 1.480%, 1.485%, 1.490%, 1.495%, 1.500%, 1.505%, 1.510%, 1.515%, 1.520%, 1.525%, 1.530%, 1.535%, 1.540%, 1.545%, 1.550%, 1.555%, 1.560%, 1.565%, 1.570%, 1.575%, 1.580%, 1.585%, 1.590%, 1.595%, 1.600%, 1.605%, 1.610%, 1.615%, 1.620%, 1.625%, 1.630%, 1.635%, 1.640%, 1.645%, 1.650%, 1.655%, 1.660%, 1.665%, 1.670%, 1.675%, 1.680%, 1.685%, 1.690%, 1.695%, 1.700%, 1.705%, 1.710%, 1.715%, 1.720%, 1.725%, 1.730%, 1.735%, 1.740%, 1.745%, 1.750%, 1.755%, 1.760%, 1.765%, 1.770%, 1.775%, 1.780%, 1.785%, 1.790%, 1.795%, 1.800%, 1.805%, 1.810%, 1.815%, 1.820%, 1.825%, 1.830%, 1.835%, 1.840%, 1.845%, 1.850%, 1.855%, 1.860%, 1.865%, 1.870%, 1.875%, 1.880%, 1.885%, 1.890%, 1.895%, 1.900%, 1.905%, 1.910%, 1.915%, 1.920%, 1.925%, 1.930%, 1.935%, 1.940%, 1.945%, 1.950%, 1.955%, 1.960%, 1.965%, 1.970%, 1.975%, 1.980%, 1.985%, 1.990%, 1.995%, or 2.000%.

[0028] According to a specific embodiment of the present disclosure, an administration dosage of the pharmaceutical composition depends on the species and weight of the subject to be treated, the nature and severity of disease, the type of formulation, administration route, and the administration period or time interval.

[0029] In a third aspect of the present disclosure, the present disclosure provides an

ophthalmic preparation for treating and/or preventing vision-impairing eye diseases. According to an embodiment of the present disclosure, a mass fraction of an active ingredient in the ophthalmic preparation ranges from 0.005% to 2%, and the active ingredient is the compound having the structure represented by Formula (I), or the nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug thereof. Through a large number of experiments, the Applicant found that such an ophthalmic preparation has a definite dose-related relaxation effect on ciliary muscle and a significant effect in delaying the ocular axis, and it can delay the progression of myopia. Therefore, the ophthalmic preparation can exert the effect of treating myopia, and allows the amblyopia trend in animal models with amblyopia gradually to recover and the incubation period to be gradually shortened. When the ophthalmic preparation is administered for a certain time, the amblyopia can be basically recovered to normal level.

[0030] According to an embodiment of the present disclosure, the above-mentioned ophthalmic preparation may further include at least one of the following additional technical features:

[0031] According to an embodiment of the present disclosure, the active ingredient is the salt of the compound represented by Formula (I), and the salt is a hydrochloride salt.

[0032] According to an embodiment of the present disclosure, the ophthalmic preparation is for use in treatment or prevention of myopia and/or amblyopia.

[0033] According to an embodiment of the present disclosure, the myopia and/or amblyopia includes one or more of mild myopia, moderate myopia, high myopia, axial myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, fundus damage, visual distortion, double vision, abnormal color vision, abnormal light vision, decreased contrast sensitivity, and ametropic amblyopia. It should be noted that the vision-impairing eye diseases described herein do not include vision problems caused by trauma.

[0034] Additional aspects and advantages of the present disclosure will be set forth in part in the description which follows and, in part, will be apparent from the description, or may be learned by practice of the present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] FIG. 1 shows a change of relative crystalline lens thickness in respective groups before and after the administration (Mean ± SD, n = 6 eyes/group);

[0036] FIG. 2 shows a change of relative pupil diameter in respective groups before and after the administration (Mean ± SD, n = 6 eyes/group).

DETAILLED DESCRIPTION

[0037] Hereinafter, embodiments of the present disclosure will be described in detail. The embodiments described below are exemplary and illustrative only and are not to be construed as limiting the present disclosure. Where specific techniques or conditions are not specified in the embodiments, they are performed according to techniques or conditions described in the literature in the art or according to the product description. The reagents or instruments used are conventional products that can be obtained commercially without indicating the manufacturer.

[0038] Furthermore, the terms "first" and "second" are used for descriptive purposes only and shall not be construed as indicating or implying relative importance or implicitly indicating the number of technical features indicated. Thus, a feature defined with "first" or "second" may explicitly or implicitly comprise at least one such feature. In the present disclosure, the meaning of "plurality" is at least two, for example, two, three, etc., unless clearly and specifically limited otherwise.

Pharmaceutical use

[0039] The uses of the compound having the structure represented by Formula (I), or the nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug thereof, according to the present disclosure, in the preparation of the medicament include: the preparation of a medicament for treating, preventing, ameliorating, controlling or alleviating the vision-impairing diseases in mammals, especially humans, and the preparation of other medicaments with insignificant toxic side effects for inhibiting M receptors.

[0040] The term “solvate” in the present disclosure indicate that the compound has a solvent on surface, in crystal lattice, or both on the surface and in the crystal lattice. A specific example

of solvate is a hydrate, in which the solvent on the surface, in the crystal lattice, or both is water. Hydrates may or may not have other solvents than water on the surface, in the crystal lattice, or both.

[0041] The term "metabolite" in the present disclosure refers to a product of metabolism of the compound having the structure represented by Formula (I) or the salt thereof in the body. Metabolites of the compound can be identified by known techniques, and the activity thereof can be characterized by assay as described herein. As used herein, the "pharmaceutically acceptable salts" refer to organic and inorganic salts of the compounds according to the present disclosure.

[0042] As used herein, the term "prodrug" refers to a compound that can be converted in vivo to the compound represented by Formula (I). Such a conversion is affected by hydrolysis of the prodrug in blood or by enzymatic conversion of the prodrug to the parent structure in blood or tissue.

Pharmaceutical compositions

[0043] As used herein, the term "composition" refers to a product comprising the specified ingredients in the specified amounts, as well as any product that is directly or indirectly resulted from combination of the specified ingredients in the specified amounts. The term associated with the pharmaceutical composition is intended to encompass the products containing one or more active ingredients, and one or more inert ingredients that make up the carrier, as well as any products that are directly or indirectly resulted from combination, complexation or aggregation of any two or more of the ingredients, or from dissociation of one or more of the ingredients, or from other types of reactions or interactions of one or more of the ingredients. Accordingly, the pharmaceutical composition according to the present disclosure encompasses any composition prepared by mixing the compound according to the present disclosure and a pharmaceutically acceptable carrier.

[0044] The pharmaceutical composition provided by the present disclosure includes at least one pharmaceutically acceptable carrier. For example, a formulation of the pharmaceutical composition is an ophthalmic preparation such as eye drops, eye ointment, eye cream, eye emulsion, eye gel, eye pills, eye film, intraocular implant.

[0045] The pharmaceutical composition provided by the present disclosure may further

includes carriers such as suitable antimicrobial agents or preservatives, suitable isotonic agents, suitable antioxidants, suitable local anesthetics, suitable suspending and dispersing agents, suitable emulsifying agents, suitable sequestering agents or chelating agents, suitable pH-adjusting agents, etc.

[0046] The pharmaceutical composition according to the present disclosure can be used in veterinary treatment of mammals such as pets, introduced species, and farm animals, in addition to being beneficial for vision-impairing eye diseases of human beings. Examples of additional animals include horses, dogs, and cats. The compound according to the present disclosure includes pharmaceutically acceptable derivatives thereof.

[0047] The present disclosure is further described with reference to specific embodiments, which are merely for illustration rather than limiting the present disclosure.

[0048] It should be understood that the data results in the following examples are all presented in Mean ± SD.

Examples: Preparation of Penehyclidine Hydrochloride Solution, as Samples for Test

[0049] Penehyclidine hydrochloride and normal saline were mixed and stirred until completely dissolved, to prepare 0.01%, 0.1%, 0.5%, 1% and 2% penehyclidine hydrochloride solutions as samples for test, respectively.

Effect Examples

Effect Example 1: Effects of Penehyclidine Hydrochloride on Crystalline Lens and Pupils of Monkeys

[0050] Healthy Cynomolgus monkeys qualified for yearly quarantine inspection, aged 2.5 to 3.5 years, weighing 2.0 to 4.0 kg, male or female, were selected and randomly divided into 6 groups, 3 monkeys in each group, with a total of 18 monkeys. The first, second, and third groups were administrated with 1%, 0.1% and 0.01% atropine sulfate eye drops, respectively. The 1%, 0.1% and 0.01% atropine sulfate eye drops were prepared by diluting the commercially available 1% atropine sulfate eye drops with PBS to different concentrations. The fourth, fifth, and sixth groups were administrated with 1%, 0.1% and 0.01% penehyclidine hydrochloride solutions, for both eyes each time, 30 μL/eye. Before the administration and at 1h, 2h, 4h, 6h, 24h, D3, D5, D7, D13 and D15 after the administration, the crystalline lens thickness and pupil diameter of both eyes were examined using A-ultrasound, and the relative crystalline lens

thickness and pupil diameter (Mean ± SD, n = 6 eyes/group) were calculated by taking the data before the administration as criteria. The results are shown in FIG. 1 and FIG. 2.

[0051] The results of lens thickness are shown in FIG. 1. At 6h after the administration, the crystalline lens thickness of each group was decreased to the minimum. The higher the concentration, the stronger the effect of reducing the crystalline lens thickness. The effects of reducing lens thickness at 6h after the administration are ranked in such an order of 1% sample for test> 0.1% sample for test ≈ 1% atropine> 0.01% sample for test> 0.1% atropine> 0.01% atropine. Each group was gradually recovered from D1. The lower the concentration, the faster the recovery. The groups administrated with the samples for test with the concentrations from 0.01% to 0.1% and the atropine group were completely recovered in 3 to 5 days after the administration, and the group administrated with the sample for test with the concentration 1% and the group administrated with 1% atropine did not completely recover in 14 days after the administration. Penehyclidine hydrochloride has a definite dose-related relaxation effect on the ciliary muscle in vivo, which can delay the progression of myopia and achieve the treatment of myopia, and it has stronger effect than atropine.

[0052] Pupil diameter results are shown in FIG. 2. The group administrated with 0.01% sample for test did not produce mydriasis. Pupil diameter in other groups showed dose-related expansion, reaching the maximum value at 6h after the administration. The effects of mydriasis are ranked in such an order of 1% atropine> 0.1% atropine> 1% sample for test> 0.01% atropine> 0.1% sample for test. After 6h, the subjects were slowly recovered from mydriasis. The groups administrated with 0.1% to 1% samples for test and the group administrated with 0.01% atropine were recovered to the normal 2 to 4 days after the administration (D3-D5), and the group administrated with 0.1% to 1% atropine were not completely recovered 14 days after the administration (D15). Compared with the atropine groups, the mydriatic side effects in the group administrated with 0.1% to 1% samples for test were significantly reduced and the recovery time was shorter, indicating that the side effects of photophobia and blurred vision caused by pupil dilation can be significantly reduced.

[0053] Effect Example 2: Treatment of Visual form deprivation Myopia in Guinea Pigs with penehyclidine hydrochloride

[0054] Two-week-old weaned, healthy short-hair tricolor guinea pigs, male or female, were

selected. After passing quarantine, 48 guinea pigs with monocular diopter of ≥ +1.00D and binocular anisometropia of ≤ 1.50D were selected and randomly divided into 6 groups: groups administrated with samples for test (high, medium and low dose), negative control group, and positive control group (atropine group), with 8 animals in each group. All animals were modeled at the left eye, and the right eye was not treated. The modeling method was isoflurane inhalation anesthesia, and the nylon fastener bottom surface of the self-made styrene plastic diffuser was adhered to the skin around the eyes by using cyanoacrylate glue. The adhesion was confirmed to be firm. The diffuser could be freely disassembled and installed. There was no light leakage except the diffuser. The disinfection and surgical procedures were controlled within 3 to 5 min. The animals were awakened after 5 to 10 min. On the modeling day, 0.01%, 0.1%, 0.5% and 1% penehyclidine hydrochloride solution, 1% atropine sulfate eye drops and phosphate buffer solution (PBS) were administered to the conjunctival sac of modeled eyes, once a day, 20 μL/eye/time, continuously administrated for 6 weeks. The animal status and diffuser adhesion status were observed once daily during the test. Diopter and ocular axis length were measured respectively before the test (D-1), two weeks after the test (D14), four weeks after the test (D28) and six weeks after the test (D42) by using retinoscopy and A-ultrasound. The results are shown in Table 1 and Table 2.

[0055] [Table 1] Results of diopter

Group		Control eyes-OD				Modeled eyes-OS			
		D-1	2 weeks	4 weeks	6 weeks	D-1	2 weeks	4 weeks	6 weeks
PBS	Mean ± SD	5.25 ±1.95	4.69 ±1.83	4.75 ±1.85	4.75 ±2.00	5.13 ±1.79	-2.69±3.21a	-4.00±3.34a	-5.06±1.04a
1% atropine	Mean ± SD	5.21 ±1.45	4.88 ±1.28	4.96 ±1.32	4.83 ±1.37	5.00 ±1.64	-0.03±2.25ab	-0.89±2.47ab	-1.18±2.52ab
1% sample for test	Mean ± SD	5.05 ±1.05	4.85 ±1.06	4.98 ±1.12	4.85 ±1.05	5.08 ±1.14	-0.05±1.80ab	-0.08±1.45ab	-0.28±1.79ab
0.5% sample for test	Mean ± SD	5.17 ±1.50	4.88 ±1.38	4.96 ±1.29	4.88 ±1.32	4.83 ±1.27	-0.03±2.91ab	-0.13±1.93ab	-0.35±1.56ab
0.1% sample for test	Mean ± SD	4.83 ±1.80	4.81 ±2.05	4.78 ±1.49	4.88 ±1.51	4.81 ±1.62	-0.08±2.57ab	-0.16±2.26ab	-0.48±1.49ab
0.01% sample for test	Mean ± SD	4.72 ±1.39	4.72 ±1.30	4.61 ±1.32	4.61 ±1.29	4.72 ±1.60	-0.09±3.18ab	-0.63±2.76ab	-1.06±2.48ab

Note: a indicates $p \leq 0.05\%$ compared to D-1; b indicates $p \leq 0.05\%$ compared to concurrent PBS group.

[0056] The diopter results are shown in Table 1. Compared with D-1, the diopter values of the modeled eyes at different time periods were statistically different. 2 weeks after the administration, the modeled eyes of animals in the group administrated with PBS eye drops induced relative myopia of -2.69 ± 3.21D, and the diopter of each dose group shifted toward myopia, but no relative myopia was induced. The relative myopia degree of modeled eyes in the PBS group increased with time, while that in other groups increased slightly. After administration for 6 weeks, relative myopia of -5.06 ± 1.04D was induced in the modeled eyes of the animals in the group administrated with PBS eye drops. The group administrated with 1% atropine eye drops and the groups administrated with 1%, 0.5%, 0.1% and 0.01% penehyclidine hydrochloride solutions were induced with relative myopia of -1.18 ± 2.52D, -0.28 ± 1.79D, -0.35 ± 1.56D, -0.48 ± 1.49D, and -1.06 ± 2.48D, respectively. The diopter values of each group were significantly lower than that of PBS group (P <0.05%). The results indicate that each treatment group had a significant effect on the treatment of myopia, and the groups administrated with sample for test at different concentrations had lower relative myopia degrees, and has stronger effect on the treatment of myopia than the group administrated with 1% atropine.

[0057] [Table 2] Result of ocular axis elongation

	Ocular axis elongation with respect to control eyes (OD) (mm)			Ocular axis elongation in modeled eyes (OS) (mm)		
	2 weeks	4 weeks	6 weeks	2 weeks	4 weeks	6 weeks
PBS	0.36 ±0.22	0.50 ±0.26	0.72 ±0.22	0.52 ±0.13a	0.68 ±0.11a	0.94 ±0.12a
1% atropine	0.29 ±0.14	0.43 ±0.21	0.72 ±0.17	0.48 ±0.19a	0.64 ±0.21a	0.82 ±0.15
1% sample for test	0.31 ±0.12	0.45 ±0.11	0.69 ±0.14	0.46 ±0.12a	0.50 ±0.13b	0.66 ±0.16b
0.5% sample for test	0.25 ±0.11	0.42 ±0.11	0.63 ±0.15	0.47 ±0.15a	0.48 ±0.12b	0.76 ±0.15b
0.1% sample for test	0.26 ±0.15	0.42 ±0.15	0.65 ±0.20	0.41 ±0.19a	0.46 ±0.16b	0.70 ±0.16b
0.01% sample for test	0.37 ±0.15	0.53 ±0.16	0.80 ±0.23	0.50 ±0.10a	0.56 ±0.15	0.82 ±0.15

Note: a indicates p <0.05% compared to OD over the same period; b indicates p <0.05% compared to PBS.

[0058] The ocular axis length of guinea pigs at D-1 was 8.2 to 8.3mm, and there was no

significant difference in the ocular axis elongation between left and right eyes in each group (P> 0.05%) and between groups (P> 0.05%). The results of ocular axis elongation are shown in Table 2. Two weeks after the administration, the ocular axis elongation of modeled eyes was significantly greater than that of OD eyes (P <0.05%), indicating that modeling caused significant axial length growth in addition to normal ocular axis elongation.

[0059] Four weeks after the administration, the ocular axis elongation of OS eyes in PBS group and 1% atropine group was still significantly greater than that of OD eyes in the same period (P <0.05%), and there was no significant difference between the groups administrated with 0.01% to 1% samples for test and OD eyes in the same period (P> 0.05%). Ocular axis elongation in OS eyes in the groups administrated with 1.0, 0.5%, and 0.1% samples for test was significantly smaller than that in OS eyes in PBS group (P <0.05%), indicating that the groups administrated with samples for test at respective concentrations significantly delayed the ocular axis elongation earlier than that in atropine group.

[0060] Six weeks after the administration, the ocular axis elongation of OS eyes in the PBS group was still significantly greater than that in OD eyes in the same period (P <0.05%). There was no significant difference in ocular axis elongation of OS eyes in each dose group and OD eyes in the same period (P> 0.05%). Axial grow in OS eyes in the groups administrated with 1.0, 0.5%, and 0.1% samples for test was significantly smaller than OS eyes in the PBS group (P <0.05%). The ocular axis elongation of the OS eyes in the group administrated with 0.01% sample for test and the ocular axis elongation of the group administrated with 1% atropine were not significantly different from that of the OS eyes in the PBS group (P> 0.05%), indicating that each dose group had the effect of delaying the ocular axis elongation, and the ocular axis elongation in the groups administrated with 0.1% to 1% samples for test was smaller, indicating the stronger effect of treating myopia than that of 1% atropine.

[0061] In conclusion, the 0.01%~1% penehyclidine hydrochloride solution provided by the embodiments of the present disclosure can effectively treat the progression of myopia, and is more effective than 1% atropine sulfate eye drop.

[0062] Effect Example 3: Investigation on Penehyclidine Hydrochloride in Treatment of Amblyopia of Cats

[0063] Twenty-four common 4-week-old domestic cats were randomly divided into a PBS

group, a test group administrated with 1% penehyclidine hydrochloride solution, a test group administrated with 2% penehyclidine hydrochloride solution, and a control group administrated with 1% atropine, with 6 cats in each group. The right lateral rectus muscle of the cats in each group was cut off at 4 weeks of age. After the formation of amblyopia was determined by pattern visual evoked potential (P-VEP) test at 4 weeks after surgery, phosphate buffer solution (PBS), 1% and 2% samples for test, 1% atropine sulfate eye drops were respectively administered through conjunctival sac eye drops once a day, 20 μL/eye/time for 12 weeks successively. The P-VEP was recorded every 4 weeks. The results are shown in Table 3.

[0064] [Table 3] P-VEP Results

Time	Group	PBS group	1% sample for test	2% sample for test	1% atropine
Before modeling	Latency (ms)	48.65 ±2.3	48.43 ±3.4	48.58 ±2.5	48.60 ±4.0
	Amplitude (nv)	55.65 ±3.2	55.58 ±3.5	55.78 ±2.9	55.46 ±3.5
4 weeks after modeling (Pre-treatment)	Latency (ms)	58.23 ±4.5	58.45 ±5.2	58.32 ±5.0	58.15 ±4.9
	Amplitude (nv)	38.24 ±2.9	38.12 ±1.8	38.05 ±2.1	39.07 ±1.9
4 weeks after treatment	Latency (ms)	59.75 ±4.1	57.33 ±4.3	56.39 ±2.5	57.67 ±2.3
	Amplitude (nv)	32.34 ±2.8	42.72 ±3.6	43.98 ±3.6	41.79 ±2.9
8 weeks after treatment	Latency (ms)	62.39 ±3.4	55.26 ±4.5	54.45 ±3.2	56.58 ±3.2
	Amplitude (nv)	27.55 ±2.9	48.72 ±3.6	50.54 ±3.4	47.65 ±2.7
12 weeks after treatment	Latency (ms)	64.23 ±3.2	51.03 ±4.3	50.25 ±3.5	54.36 ±4.6
	Amplitude (nv)	20.34 ±2.8	52.55 ±3.1	53.67 ±3.1	50.78 ±3.8

[0065] As shown in Table 3, the latency and amplitude (nv) of P wave in each group were basically the same before modeling. After 4 weeks of modeling, the latency of P-VEP in each group was significantly prolonged and the amplitude was significantly reduced, which were statistically significant compared with those before modeling, indicating that the animal model of amblyopia was successfully created in each group after 4 weeks of right lateral rectus amputation. The latency of P-VEP in the PBS group continued to extend and the amplitude continued to decrease during continuous administration for 4 to 12 weeks. The P-VEP trend in each treatment group was gradually recovered, the latency was gradually shortened, and the amplitude was gradually increased. Twelve weeks after the administration, the groups administrated with 1% and 2% samples for test were almost recovered to pre-modeling, and the

amblyopia recovery effect of the groups administrated with 1% and 2% samples for test was higher than that of the group administrated with 1% atropine. The results indicate that 1% to 2% penehyclidine hydrochloride solutions had better effect on amblyopia than atropine.

[0066] Effect Example 4: Investigation on Repeated Eye Drop Toxicity of Penehyclidine Hydrochloride in Rabbits

[0067] 30 healthy Dutch rabbits in total, male or female, qualified after quarantine, were selected and randomly divided into 5 groups, 6 rabbits in each group, including a solvent control group, a control group administrated with 1% atropine, test groups respectively administrated with 0.01%, 1% and 2% penehyclidine hydrochloride solutions. The animals were administered with eye drops in bilateral conjunctival sac once a day, 30 μL/eye/time, repeated for 12 weeks. All animals were observed for death, morbidity, respiration, secretions, feces, diet and drinking at least once daily during the test. Each animal was visually observed for pupillary light reflex prior to each administration, and eye irritation was observed within 1 minute after each administration, including, but not limited to, squinting, blinking and head flick. If the animal is found with any of these abnormalities, the frequency (counts per minute) and/or duration (recorded as shorter than or longer than 60 seconds) of occurrence is recorded. Prior to administration in D1, 4-th week, 8-th week and 12-th week, all animals received local observation on eyes, including, but not limited to, redness, swelling, conjunctival hyperemia and secretion. The anterior segment and fundus were examined by using hand-held slit lamp and direct ophthalmoscope. The results are shown in Table 4 to Table 6.

[0068] [Table 4] Eye Irritation Results

	Squinting		Blinking		Throwing head		Reflection of light in pupils	Status
Group	Frequency	Duration	Frequency	Duration	Frequency	Duration		
Solvent control group	√	√	√	√	√	√	√	√
1% atropine group	13	L	16	L	√	√	Disappear	√
Group administrated with 2% sample for test	3	S	4	S	√	√	Decrease	√
Group administrated with 1% sample for test	√	√	√	√	√	√	√	√
Group administrated with 0.01% sample for test	√	√	√	√	√	√	√	√

Note: frequency means times per minute, S means duration shorter than 60s, L means duration longer than 60s, √ means no abnormality.

[0069] As shown in Table 4, the eye irritation results indicate that 1% atropine group showed moderate irritation, and the reflection to light by pupils disappeared. Except the slight irritation and reduced reflection to light in the pupils in 2% high-dose group, the groups administrated with 1% and 0.01% samples for test exhibited no irritation, and similar to the solvent control group, they had normal reflection to light in the pupils, indicating that penehyclidine hydrochloride is safe in ocular administration and had insignificant effects on pupils.

[0070] [Table 5] Ophthalmic Examination Results

Time		Solvent control group	1% atropine group	Group administrated with 2% sample for test	Group administrated with 1% sample for test	Group administrated with 0.01% sample for test
D1	Corneal opacity	0	0	0	0	0
	Conjunctival chemosis	0	0	0	0	0
	Intraocular pressure	17	25	18	16	17
4-th week	Corneal opacity	0	1	0	0	0
	Conjunctival chemosis	0	0	0	0	0
	Intraocular pressure	18	23	16	17	17
8-th week	Corneal opacity	0	1	0	0	0
	Conjunctival chemosis	0	1	0	0	0
	Intraocular pressure	16	26	17	16	18
12-th week	Corneal opacity	0	1	0	0	0
	Conjunctival chemosis	0	1	0	0	0
	Intraocular pressure	18	24	18	17	17

[0071] [Table 6] Results of ocular local observations

Corneal opacity (% range)		Conjunctival chemosis and swelling	
0	Cornea was normal without turbidity	0	Normal, no edema
1	1% to 25% area of visible substrate turbidity	1	Slight edema, no eyelid eversion

2	26% to 50% area of visible substrate turbidity	2	Moderate edema resulting in incomplete upper and lower eyelid closure; edema was confined to the upper eyelid, which was partially everted
3	51% to 75% area of visible substrate turbidity	3	Obvious edema accompanied with partial eversion of the upper and lower eyelids, position of which were easily determined by frontal observation and observation of the eyelid position
4	76% to 100% area of visible substrate turbidity	4	Significant upper and lower eyelid eversion, upper eyelid more obvious than lower eyelid, difficult to recover

[0072] As shown in Table 6, after repeated administration of samples for test at different concentrations for 12 weeks, no corneal opacity and conjunctival chemosis were observed, and intraocular pressure was similar to the solvent control group. However, 4 weeks after the repeated administration, slight corneal opacity and slight conjunctival edema were observed in the atropine group, indicating that the safety of repeated administration of penehyclidine hydrochloride was significantly superior to that of atropine at the same concentration.

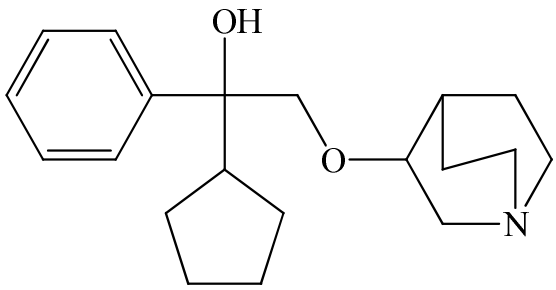
[0073] In the specification, references to descriptions of the terms "an embodiment", "some embodiments", "examples", "specific examples", or "some examples", etc. mean that a particular feature, structure, material, or characteristic described in connection with the embodiment or example is included in at least one embodiment or example of the present disclosure. In this specification, schematic representations of the terms are not necessarily directed to the same embodiment or example. Furthermore, the particular features, structures, materials, or characteristics described may be combined in any suitable manner in any one or more embodiments or examples. Furthermore, combinations and compositions of the various embodiments or examples and features of the various embodiments or examples described in this specification can be made by those skilled in the art without contradiction among each other.

[0074] The embodiments of the present disclosure illustrated and described above are merely exemplary and not intend to limit the present disclosure. Those skilled in the art can make changes, modifications, substitutions and alterations to the above embodiments without departing from the scope of the present disclosure.

CLAIMS

What is claimed is:

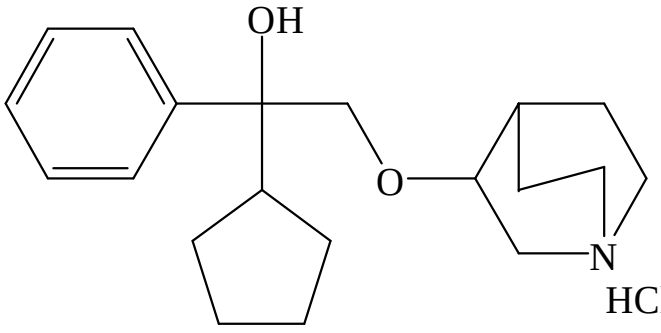
1. Use of a compound having a structure represented by Formula (I), or a nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug thereof, in the preparation of medicament for treating and/or preventing vision-impairing eye diseases,



Formula (I).

2. The use according to claim 1, wherein the salt of the compound represented by Formula (I) is selected from organic salts or inorganic salts.

3. The use according to claim 1, wherein the salt of the compound represented by Formula (I) is a hydrochloride salt, and preferably, the hydrochloride salt has a structure represented by Formula (II),



Formula (II).

4. The use according to claim 1, wherein the medicament is for use in the treatment and/or prevention of myopia and/or amblyopia.

5. The use according to claim 1, wherein the medicament is for use in the treatment and/or prevention of myopia and/or amblyopia, the myopia and/or amblyopia comprising one or more of mild myopia, moderate myopia, high myopia, axial myopia, refractive myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, ocular axis elongation, fundus damage, visual distortion, double vision, abnormal color vision,

abnormal light vision, decreased contrast sensitivity, anisometropic amblyopia, ametropic amblyopia, unilateral visual form deprivation amblyopia, or bilateral visual form deprivation amblyopia.

6. A pharmaceutical composition for treating and/or preventing vision-impairing eye diseases, wherein the pharmaceutical composition comprises, as an active ingredient, the compound having the structure represented by Formula (I), or the nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug thereof according to claim 1.

7. The pharmaceutical composition according to claim 6, wherein the pharmaceutical composition further comprises at least one pharmaceutically acceptable carrier.

8. The pharmaceutical composition according to claim 6, wherein the pharmaceutical composition is in a formulation of an ophthalmic preparation, the ophthalmic preparation comprising one or more of eye drops, eye ointment, eye cream, eye emulsion, eye gel, eye pills, eye film, or intraocular implant.

9. The pharmaceutical composition according to claim 6, wherein a mass fraction of the active ingredient in the pharmaceutical composition ranges from 0.005% to 2%, based on a mass of the pharmaceutical composition.

10. The pharmaceutical composition according to any one of claims 6 to 9, wherein the pharmaceutical composition is for use in the treatment or prevention of myopia and/or amblyopia.

11. The pharmaceutical composition according to claim 10, wherein the myopia and/or amblyopia comprises one or more of mild myopia, moderate myopia, high myopia, axial myopia, refractive myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, ocular axis elongation, fundus damage, visual distortion, double vision, abnormal color vision, abnormal light vision, decreased contrast sensitivity, anisometropic amblyopia, ametropic amblyopia, unilateral visual form deprivation amblyopia, or bilateral visual form deprivation amblyopia.

12. An ophthalmic preparation for treating and/or preventing vision-impairing eye diseases, wherein a mass fraction of an active ingredient in the ophthalmic preparation ranges from 0.005% to 2%, and the active ingredient is the compound having the structure represented by Formula (I), or the nitrogen oxide, solvate, metabolite, pharmaceutically acceptable salt or prodrug

thereof according to claim 1.

13. The ophthalmic preparation according to claim 12, wherein the active ingredient is a salt of the compound represented by Formula (I), and the salt is a hydrochloride salt.

14. The ophthalmic preparation according to claim 12 or 13 wherein the ophthalmic preparation is for use in the treatment or prevention of myopia and/or amblyopia.

15. The ophthalmic preparation according to claim 14, wherein the myopia and/or amblyopia comprises one or more of mild myopia, moderate myopia, high myopia, axial myopia, refractive myopia, simple myopia, pathological myopia, distance vision loss, asthenopia, exotropia, strabismus amblyopia, ocular axis elongation, fundus damage, visual distortion, double vision, abnormal color vision, abnormal light vision, decreased contrast sensitivity, anisometropic amblyopia, ametropic amblyopia, unilateral visual form deprivation amblyopia, or bilateral visual form deprivation amblyopia.