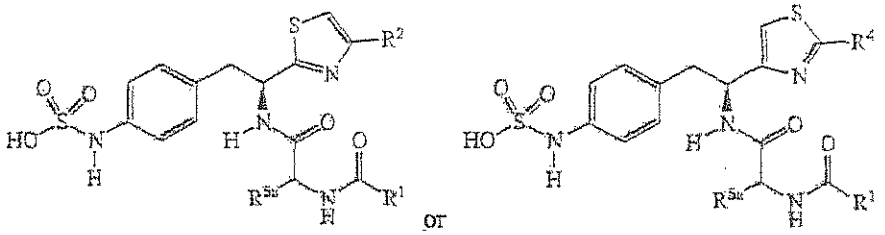
monitoring the level of Ang-2 and administering the appropriate amount of HPTP-β inhibitor, either alone, or as part of a prophylactic combination therapy.

Disclosed herein is the use of a compound for making a medicament for treating vascular leak syndrome, the compound having the formula:



or

$R^2$ and $R^4$ are each independently:

i) substituted or unsubstituted $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or C3-$C_6$ cyclic alkyl;

ii) substituted or unsubstituted phenyl; or

iii) substituted or unsubstituted heteroaryl;

wherein the substitutions are chosen from $C_1 - C_4$ linear or branched alkyl, $C_1$-$C_4$ linear or branched alkoxy and halogen;

$R^1$ is chosen from:

i) $C_1$-$C_6$ linear, $C_3 - C_6$ branched, or $C_3$-$C_6$ cyclic alkyl; or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkoxy;

$R^{5a}$ is:

i) hydrogen;

ii) $C_1$-$C_6$ linear or $C_3$-$C_6$ branched alkyl; or

iii) a unit having the formula:

$$-[C(R^{7a}H)]_tR^8$$

$R^{7a}$ is

i) hydrogen; or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or C3-$C_6$ cyclic alkyl;

$R^8$ is:

i) hydrogen;

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or C3-$C_6$ cyclic alkyl; or

iii) phenyl;

the index t is 0 to 4; or

a pharmaceutically acceptable salt thereof.

## BRIEF DESCRIPTION OF THE FIGURES

**Figure 1** depicts the effect of 4-{(*S*)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ammonium salt (inhibitor) on murine blood pressure during IL-2 induced VLS at low and high IL-2 dosing. As depicted, High IL-2 dosing in the absence of a Tie-2 signal amplifier resulted in death. A depicts the control sample; B depicts mice treated with 180,000 IU of IL-2 for 5 days; C depicts mice treated with 180,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days; D depicts mice treated with 400,000 IU of IL-2 for 5 days; E depicts mice treated with 400,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days.

**Figure 2** depicts the effect of 4-{(*S*)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ammonium salt, a Tie-2 signal amplifier, on IL-2 induced shock in mice. A depicts the control sample; B depicts mice treated with 180,000 IU of IL-2 for 5 days; C depicts mice treated with 180,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days; D depicts mice treated with 400,000 IU of IL-2 for 5 days; E depicts mice treated with 400,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days.

**Figure 3** depicts the effect of 4-{(*S*)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ammonium salt, a Tie-2 signal amplifier, on IL-2 induced murine mortality. A depicts the control sample; B depicts mice treated with 180,000 IU of IL-2 for 5 days; C depicts mice treated with 180,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days; D depicts mice treated with 400,000 IU of IL-2 for 5 days; E depicts mice treated with 400,000 IU of IL-2 for 5 days and 40 mg/kg of D91 for the first 2 days, then at 20 mg/kg for 3 days.

**Figure 4** depicts the status of the animals of each group after treatment with High IL-2 dosing with and without the Tie-2 signal amplifier, 4-{(*S*)-2-[(*S*)-2-(methoxycarbonylamino)-3-phenyl-propanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid ammonium salt. A depicts the control sample; B depicts the status of mice treated with 400,000 IU of IL-2

4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonyl)-4-methylpentanamido]-2-(4-ethylthiazol-2-yl)ethyl}phenylsulfamic acid;

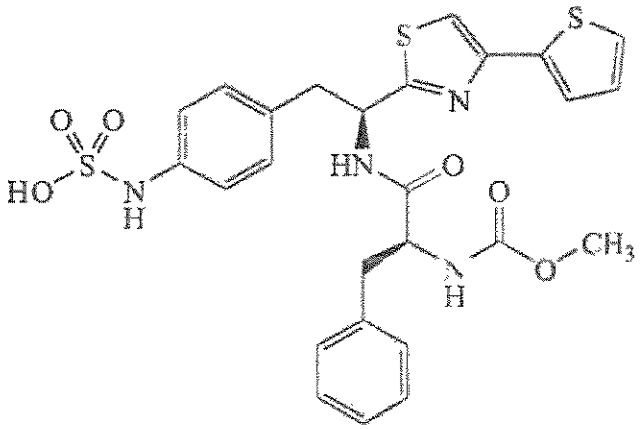
4-{(*S*)-2-(4-Ethylthiazol-2-yl)-2-[(*S*)-2-(methoxycarbonyl)-4-methylpentanamido]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(*tert*-Butoxycarbonyl)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl]ethyl}phenylsulfamic acid;

4-{(*S*)-2-[(*S*)-2-(Methoxycarbonyl)-4-methylpentanamido]-2-[2-(thiophen-2-yl)thiazol-4-yl)ethyl}phenylsulfamic acid; and

(*S*)-4-{2-[2-(*tert*-Butoxycarbonyl)acetamide]-2-(4-ethylthiazol-2-yl)ethyl}-phenylsulfamic acid.

27. The use according to any of Claim 1 to 15, wherein the compound has the formula:



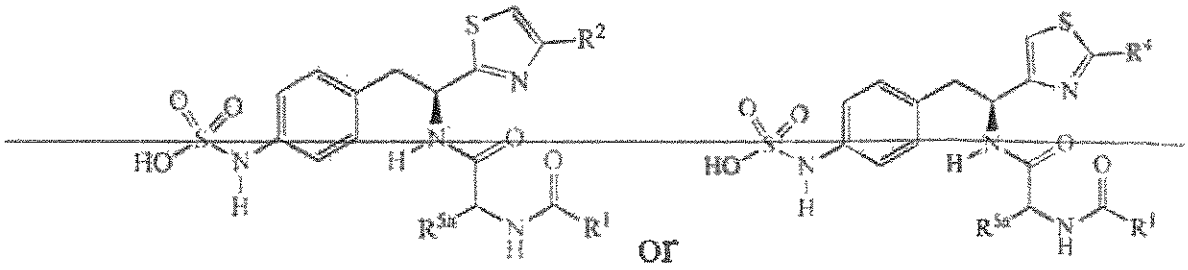
; and

pharmaceutically acceptable salts thereof.

28. The use according to any of Claim 1 to 15 and 16 to 53, wherein the compound is in the form of a salt of a cation chosen from ammonium, sodium, lithium, potassium, calcium, magnesium, bismuth, and lysine.

~~29. A composition for providing vascular stabilization in a subject, comprising:~~

~~A) an effective amount of one or more compounds having the formula~~



or

$R^2$ and $R^4$ are each independently:

i) substituted or unsubstituted $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

ii) substituted or unsubstituted phenyl; or

iii) substituted or unsubstituted heteroaryl;

wherein the substitutions are chosen from $C_1$-$C_4$ linear or branched alkyl, $C_1$-$C_4$ linear or branched alkoxy and halogen;

$R^1$ is chosen from:

i) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkoxy;

$R^{5a}$ is:

i) hydrogen;

ii) $C_1$-$C_6$ linear or $C_3$-$C_6$ branched alkyl; or

iii) a unit having the formula:

$$-[C(R^{7a}H)]_tR^8$$

$R^{7a}$ is

i) hydrogen; or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

~~$R^8$ is:~~

~~i) hydrogen;~~

~~ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;~~

~~or~~

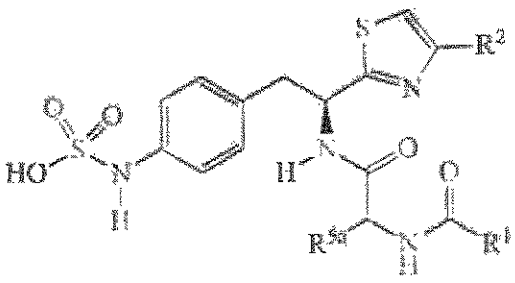
~~iii) phenyl;~~

~~the index t is 0 to 4; or~~

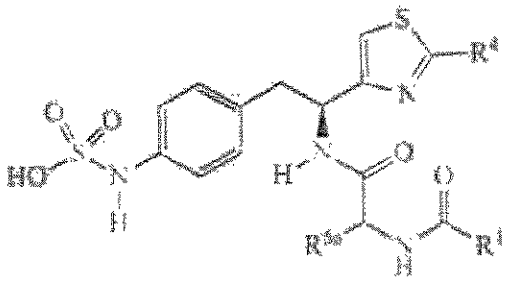
~~a pharmaceutically acceptable salt thereof; and~~

~~B) one or more pharmaceutically acceptable ingredients.~~

2930. A use of a compound for making a medicament for treating vascular leak syndrome, the compound having the formula:



or



$R^2$ and $R^4$ are each independently:

i) substituted or unsubstituted $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

ii) substituted or unsubstituted phenyl; or

iii) substituted or unsubstituted heteroaryl;

wherein the substitutions are chosen from from $C_1$-$C_4$ linear or branched alkyl, $C_1$-$C_4$ linear or branched alkoxy and halogen;

$R^1$ is chosen from:

i) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl; or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkoxy;

$R^{5a}$ is :

i) hydrogen;

ii) $C_1$-$C_6$ linear or $C_3$-$C_6$ branched alkyl; or

iii) a unit having the formula:

$$-[C(R^{7a}H)]_tR^8$$

$R^{7a}$ is

i) hydrogen; or

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

$R^8$ is:

i) hydrogen;

ii) $C_1$-$C_6$ linear, $C_3$-$C_6$ branched, or $C_3$-$C_6$ cyclic alkyl;

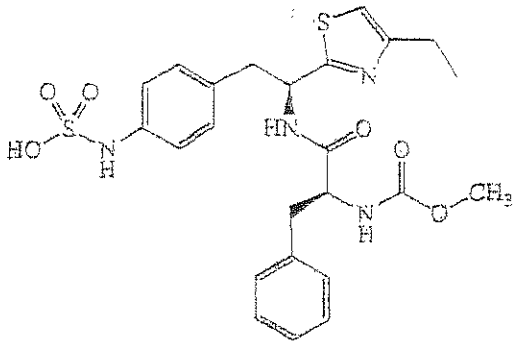
or

iii) phenyl;

the index t is 0 to 4; or

a pharmaceutically acceptable salt thereof.

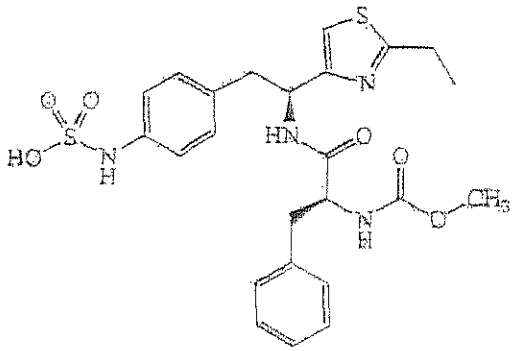
~~31.~~ 30. The medicament according to any of Claims 1-15, wherein the compound has the formula:



: and

pharmaceutically acceptable salts thereof.

~~32.~~ 31. The medicament according to any of Claims 1-15, wherein the compound has the formula:



: and

pharmaceutically acceptable salts thereof.