Summary of the Invention

Problem to be Solved by the Invention

[0007] The present invention was made in order to solve the foregoing problems, and it is an object thereof to provide a Maillard reaction inhibitor which effectively inhibits the progress of a Maillard reaction in a living body (e.g., human beings, pets, and livestock) and can be safely applied without any adverse side effects and be manufactured without requiring any complicated process, and a skin anti-aging agent, an anti-diabetic complication agent, foods and beverages using the same.

Means for Solving the Problem

[0008] The present invention provides a Maillard reaction inhibitor containing 50 to 90% by mass of polyphenol as an active ingredient.

[0009] In one embodiment, the polyphenol includes 10 to 50% by mass of ellagitannin with respect to a total mass of the polyphenol.

[0010] In a further embodiment, the ellagitannin includes at least one compound selected from the group consisting of punicalin, punicalagin, oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A and pomegraniin B~~ a compound represented by the formula (VI), and a compound represented by the formula (VII).

[0011] In one embodiment, the polyphenol is contained in the form of a polyphenol containing plant extract.

[0012] In one embodiment, the polyphenol containing plant extract is an extract derived from at least one plant selected from the group consisting of plants belonging to the genera *Punica*, *Quisqualis*, *Cistus*, *Terminalia*, and *Combretum*.

[0013] The present invention also provides a skin anti-aging agent containing the above Maillard reaction inhibitor.

[0014] The present invention also provides an anti-diabetic complication agent containing the above Maillard reaction inhibitor.

[0015] The present provides a food or beverage, to which the above Maillard

reaction inhibitor is added.

[0016] The present invention provides an external preparation, to which the above Maillard reaction inhibitor is added.

Advantageous Effects of the Invention

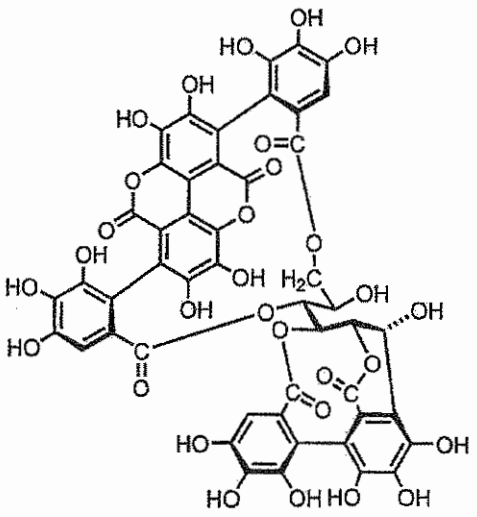
[0017] The Maillard reaction inhibitor of the present invention has a potent Maillard reaction inhibitory activity, effectively suppresses the production of AGEs, and can prevent or improve various symptoms due to AGEs. For example, the Maillard reaction inhibitor can suppress aging due to the Maillard reaction, and prevent and improve wrinkles, looseness of skin and loss of the firmness or elasticity of the skin. Also, the Maillard reaction inhibitor can effectively prevent and treat diabetic complications such as a diabetic neuropathy, diabetic nephropathy and diabetic retinopathy. Moreover, the foods and beverages of the present invention can be easily taken to suppress the occurrence or progress of the Maillard reaction in a living body because the Maillard reaction inhibitor is mixed therein. Furthermore, the foods and beverages of the present invention can also inhibit the occurrence and/or the progress of the Maillard reaction in those foods and beverages by mixing therein the Maillard reaction inhibitor together with collagen, thereby suppressing the deterioration of those foods and beverages to maintain their quality for a long time.

Brief Description of Drawings

[0018] FIG. 1 shows ^{1}H-NMR spectra for identifying a compound isolated in Example 2: (a) ^{1}H-NMR spectrum of ~~pomegraniin B~~the compound represented by the formula (VII); (b) ^{1}H-NMR spectrum of ~~pomegraniin A~~the compound represented by the formula (VI); and (c) ^{1}H-NMR spectrum of eucarbanin B.

Description of Embodiments

[0019] The Maillard reaction inhibitor of the present invention contains polyphenol as an active ingredient.



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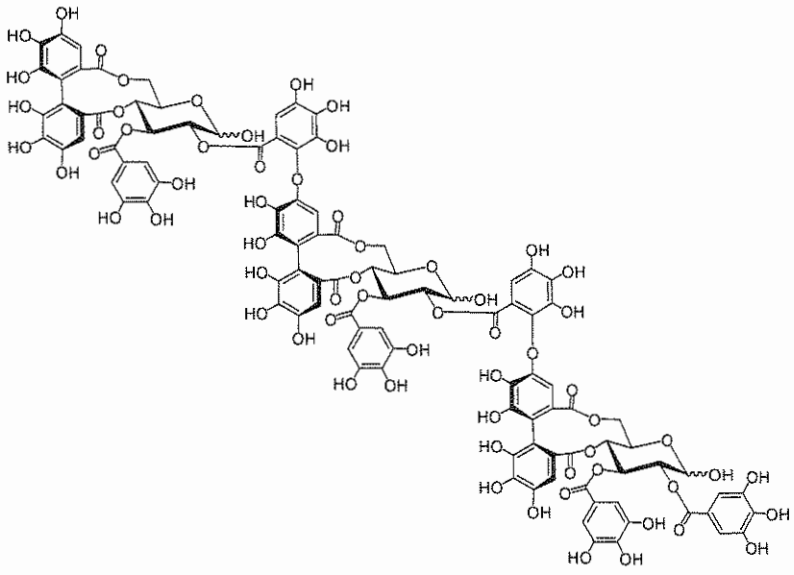
[0034] ~~pomegraniin A~~a compound represented by the following formula (VI):

[0035] [Chemical 6]



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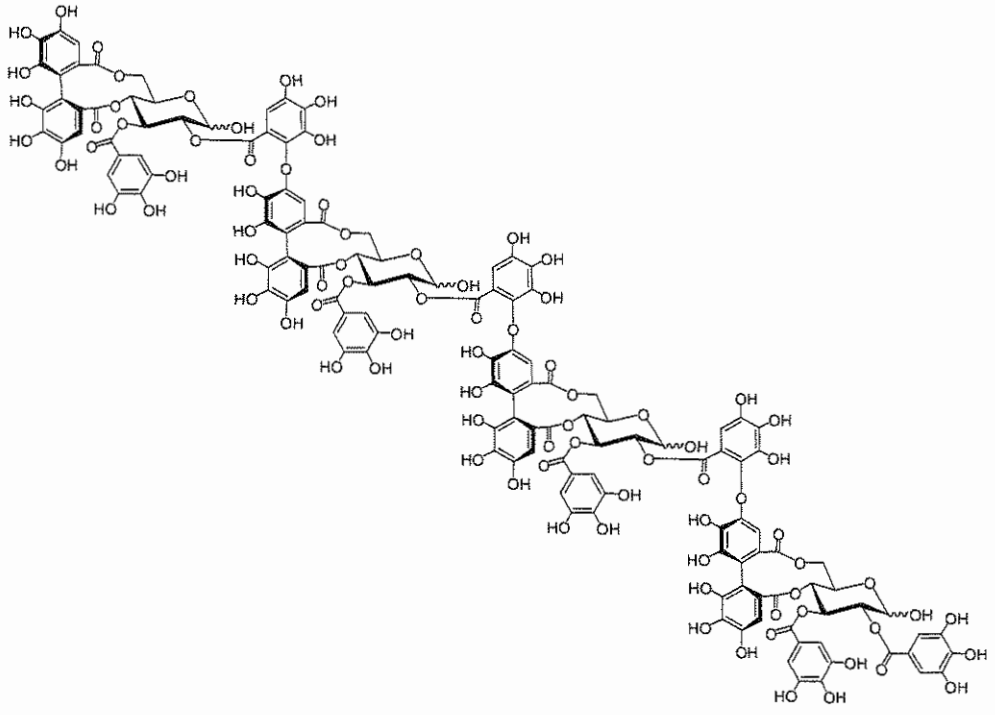
[0036] ~~pomegraniin B~~a compound represented by the following formula (VII):

[0037] [Chemical 7]



(VII)

[0038] and a combination thereof, but are not particularly limited thereto.

[0039] In the present invention, ellagitannin may be a single compound itself selected from punicalin, punicalagin, oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A~~a compound represented by the formula (VI) or ~~pomegraniin B~~a compound represented by the formula (VII) as above or a mixture thereof, or a polymer or a copolymer including at least one of punicalin, punicalagin, oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A~~a compound represented by the formula (VI) or ~~pomegraniin B~~a compound represented by the formula (VII) as a basic structure. Alternatively, ellagitannin may be a mixture of the single compound and the polymer and/or the copolymer. There is no particular limitation on degree of polymerization of ellagitannin in the form of a polymer or a copolymer, and the degree thereof is 2 to 10.

[0040] In the present invention, the above-described polyphenol is preferably contained in form of a polyphenol containing plant extract.

[0041] Examples of plants providing the polyphenol containing plant extract include, but are not particularly limited to, plants belonging to the genera *Punica*, *Quisqualis*, *Cistus*, *Terminalia*, and *Combretum*. The polyphenol containing plant extract may be a single extract obtained from the plants or a

d represents a relative value (–) of the fluorescent products of the Maillard reaction in terms of quinine sulfate when the reaction solution D is used.

[0075] Thereafter, 50% inhibition ratio (IC_{50}) of each sample was calculated as follows. That is, the inhibition ratio was plotted with respect to the sample concentration, 4-parameter plot was performed, and the concentration showing an inhibition ratio of 50% was taken as IC_{50}.

[0076] Table 2 shows the Maillard reaction inhibition ratios (%) with respect to the prepared solutions. Furthermore, Table 3 shows IC_{50} values calculated from the Maillard reaction inhibition ratios (%) with respect to the prepared solutions shown in Table 2.

[0077] [Table 2]

	Maillard reaction inhibition ratio (%)								
Conc. (mg/mL)	0.01	0.03	0.1	0.3	1	10	100	300	1000
Pomegranate extract	-	-	8.4	40.7	70.4	85.5	76.6	-	-
Punicalin	7.6	6.5	32.1	69.6	73.1	84.9	-	-	-
Punicalagin	4.3	10.9	36.2	71.4	73.5	86.1	-	-	-
Oenotein B	15.5	-	-	-	69.2	64.6	-	-	-
Eucarbanin B	-	-	21.2	-	72.9	79.4	-	-	-
Punicacortein C	-	-	39.6	-	76.8	78.2	-	-	-
~~[Pomegraniin A]~~ Compound represented by the formula (VI)	-	-	46.6	-	76.7	95.4	-	-	-
~~[Pomegraniin B]~~ Compound represented by the formula (VII)	30.4	-	40.3	-	74.3	82.5	-	-	-
Aminoguanidine	-	-	-	-	-	-	40.2	51.4	62
Tannic acid	12.7	-	48.7	-	65.1	68.8	-	-	-
Ellagic acid dihydrate	1.9	2.2	12.0	44.8	68.3	78.4	-	-	-

—: not measured

[0078] [Table 3]

	IC_{50} (mg/mL)
Pomegranate extract	0.56
Punicalin	0.16
Punicalagin	0.15
Oenotein B	0.43
Eucarbanin B	0.43
Punicacortein C	0.16
~~[Pomegraniin A]~~ Compound represented by the formula (VI)	0.13
~~[Pomegraniin B]~~ Compound represented by the formula (VII)	0.21
Aminoguanidine	273.31
Tannic acid	0.31
Ellagic acid dihydrate	0.34

[0079] As shown in Tables 2 and 3, it is found that each of the pomegranate extract, punicalin, punicalagin, oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A~~a compound represented by the formula (VI) and ~~pomegraniin B~~ a compound represented by the formula (VII) had a superior Maillard reaction inhibitory activity to aminoguanidine serving as a positive control. Furthermore, as is clear from Table 2, it is found that punicalin, punicalagin, oenotein B and a compound represented by the formula (VII) ~~pomegraniin B~~ were particularly superior in Maillard reaction inhibition ratio (%) to ellagic acid dihydrate and aminoguanidine serving as a positive control even when prepared at lower concentrations. In addition, as is clear from Tables 2 and 3, it is found that all IC_{50} values of punicalin, punicalagin, punicacortein C, ~~pomegraniin A~~ a compound represented by the formula (VI) and ~~pomegraniin B~~ a comopound represented by the formula (VII) were particularly low compared with those of tannic acid, ellagic acid dihydrate and aminoguanidine serving as a positive control, and each of them has a superior Maillard reaction inhibitory activity.

[0080] Example 2: Extraction of ellagitannin from pomegranate powder

Seven hundred milliliters of water was added to 300 g of commercially available dry pomegranate powder (made in China). The mixture was allowed to stand with stirring at 50°C for 24 hours, was allowed to cool, and

Compound	Elution time/min.
Punicalin	7.3
Punicalagin	11.2, 12.9
Oenotein B	12.1
Eucarbanin B	13.1
Punicacortein C	12.5
~~[Pomegraniin A]~~ Compound represented by the formula (VI)	12.3
~~[Pomegraniin B]~~ Compound represented by the formula (VII)	13.3
Ellagic acid dihydrate	24.3

[0088] As shown in Table 4, it is found that the sample S obtained in this example contained polyphenol, specifically certain amounts of various ellagitannins.

[0089] Moreover, the above-described sample S was subjected to the separation according to the following conditions to isolate oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A~~ a compound represented by the formula (VI) and ~~pomegraniin B~~ a compound represented by the formula (VII). Of these compounds, ~~pomegraniin A~~ a compound represented by the formula (VI), ~~pomegraniin B~~ a compound represented by the formula (VII) and eucarbanin B were identified as these compounds by ^{1}H-NMR spectrum measurement (600 MHz, acetone-d_6+D_2O) as shown in FIG. 1. ^{1}H-NMR data (600 MHz, acetone-d_6+D_2O) of ~~pomegraniins A~~ the compound represented by the formula (VI) and ~~B~~ the compound represented by the formula (VII) are shown below: 6.97-7.05 (galloyl-H), 6.11-6.67 (HHDP-H, valoneoyl-H), 5.55-5.85 (glucose H-3), 5.49-5.61 (glucose H-1 (α-anomer), H-3), 5.24-5.26 (glucose H-6), 5.03-5.22 (glucose H-1 (β-anomer), H-2, 4, 6), 4.61-4.63 (glucose H-5 (β-anomer)), 4.30-4.32 (glucose H-1 (β-anomer)), 4.08-4.26 (glucose H-5 (α-anomer)), 3.66-3.93 (glucose H-6). In addition, results of electrospray mass

spectrometry (ESI-MS) of ~~pomegraniins A~~ the compound represented by the formula (VI) and ~~B~~ the compound represented by the formula (VII) are also shown below:

~~Pomegraniin A~~ The compound represented by the formula (VI) (trimer) ESI-MS: m/z 2353 $(M-H)^-$, 1176 $(M-2H)^{2-}$

~~Pomegraniin B~~ The compound represented by the formula (VII) (tetramer) ESI-MS: m/z 3137 $(M-H)^-$, 1568 $(M-2H)^{2-}$.

[0090]<Conditions of HPLC analysis>

Detector: Ultraviolet absorption spectrometer (280nm)

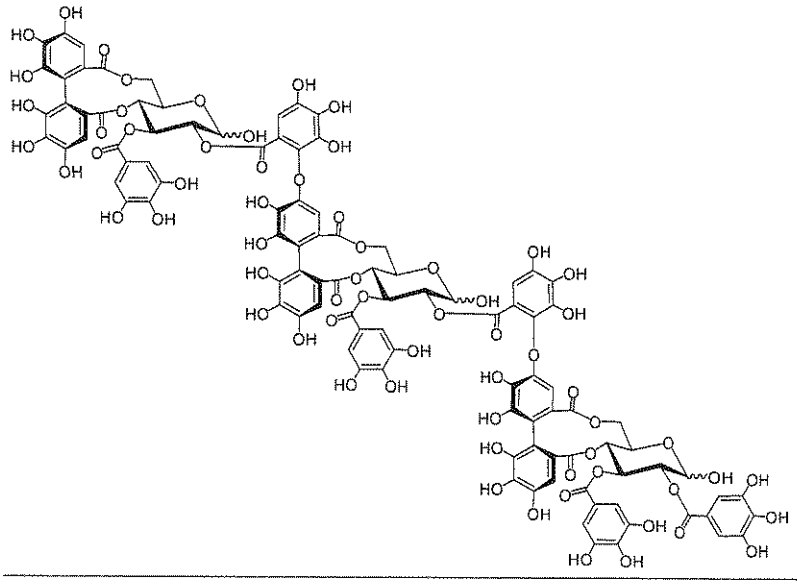
Column: YMC-Pack SIL A-003 (4.6 x 250 mm) (manufactured by YMC

CLAIMS

1. A Maillard reaction inhibitor containing 50 to 90% by mass of polyphenol as an active ingredient.

2. The Maillard reaction inhibitor according to claim 1, wherein the polyphenol includes 10 to 50% by mass of ellagitannin with respect to a total mass of the polyphenol.

3. The Maillard reaction inhibitor according to claim 2, wherein the ellagitannin comprises at least one compound selected from the group consisting of punicalin, punicalagin, oenotein B, eucarbanin B, punicacortein C, ~~pomegraniin A and pomegraniin B~~ a compound represented by the following formula (VI):



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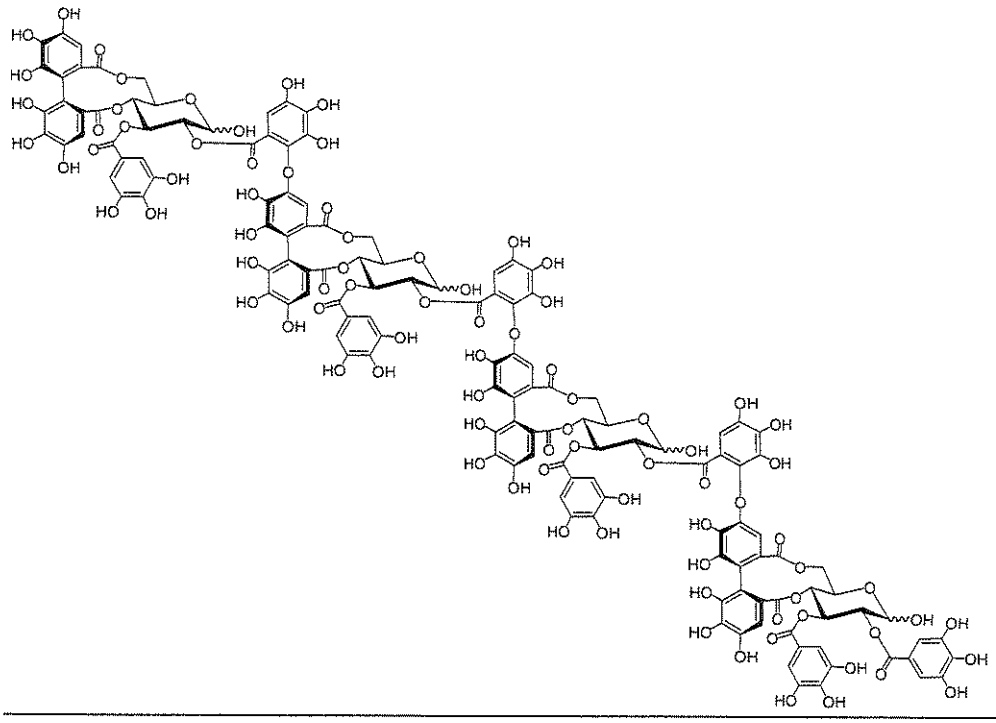
and a compound represented by the following formula (VII):



(VII).

4. The Maillard reaction inhibitor according to any one of claims 1 to 3, wherein the polyphenol is contained in the form of a polyphenol containing plant extract.

5. The Maillard reaction inhibitor according to claim 4, wherein the polyphenol containing plant extract is an extract derived from at least one plant selected from the group consisting of plants belonging to the genera *Punica*, *Quisqualis*, *Cistus*, *Terminalia*, and *Combretum*.

6. A skin anti-aging agent containing the Maillard reaction inhibitor according to any one of claims 1 to 5.

7. An anti-diabetic complication agent containing the Maillard reaction inhibitor according to any one of claims 1 to 5.

8. A food or beverage, to which the Maillard reaction inhibitor according