

TOPICAL FORMULATIONS COMPRISING STRONTIUM AND METHYLSULFONYLMETHANE (MSM) AND METHODS OF TREATMENT

FIELD OF THE INVENTION

[001] The current disclosure relates generally to topical formulations comprising
5 Strontium and Methylsulfonylmethane (MSM) and methods of treatment.

BACKGROUND OF THE INVENTION

[002] Using high concentration of active ingredients in topical cosmetic and medicinal
products produce desired results usually when a low pH is used, which may cause side
effects, such as irritation, – including stinging, burning, itching, edema, other unpleasant
10 sensations, redness, etc.

SUMMARY OF THE INVENTION

[003] In one aspect, the invention is a topical cosmetic or medicinal formulation
comprising: Strontium, Methylsulfonylmethane (MSM) and a dermatologically acceptable
carrier.
15 [004] In another aspect, the invention is a method of cosmetic treatment, comprising
topical administration of a topical formulation comprising Strontium, MSM and a
dermatologically acceptable carrier.
[005] In still another aspect, the invention is a method of reducing skin irritant effects of a
topical cosmetic or medicinal formulation or other chemical irritants, comprising strontium
20 and MSM in the cosmetic or medicinal formulation.

BRIEF DESCRIPTION OF THE DRAWINGS

[006] The subject matter regarded as the invention is particularly pointed out and distinctly
claimed in the concluding portion of the specification. The invention, however, both as to
organization and method of operation, together with objects, features, and advantages
25 thereof, may best be understood by reference to the following detailed description when read
with the accompanying drawings in which:

[007] Fig. 1 depicts comparative clinical data from Example I showing an effect on skin
redness (Δa^*) with formulations according to the invention;

- [0008] Fig. 2 depicts comparative clinical data from Example I showing an effect on overall skin color (delta E*) with formulations according to the invention;
- [0009] Fig. 3 depicts comparative clinical data from Example I showing an effect on skin irritation level with formulations according to the invention;
- 5 [0010] Fig. 4 depicts a comparison of the data shown in table 1;
- [0011] Fig. 5 depicts a comparison of improvement-from-baseline of the data shown in table 1;
- [0012] Fig. 6 depicts comparative clinical data from Example II showing an effect on skin redness (delta a*) with formulations according to the invention;
- 10 [0013] Fig. 7 depicts comparative clinical data from Example II showing an effect on overall skin color (delta E*) with formulations according to the invention;
- [0014] Fig. 8 depicts comparative clinical data from Example II showing an effect on skin irritation level with formulations according to the invention;
- [0015] Fig. 9 depicts a comparison of the data shown in table 2; and
- 15 [0016] Fig. 10 depicts a comparison of improvement-from-baseline of the data shown in table 2.

[0017] It will be appreciated that for simplicity and clarity of illustration, elements shown in the figures have not necessarily been drawn to scale. For example, the dimensions of some of the elements may be exaggerated relative to other elements for clarity. Further, where considered appropriate, reference numerals may be repeated among the figures to indicate corresponding or analogous elements.

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DETAILED DESCRIPTION OF THE PRESENT INVENTION

[0018] In the following detailed description, numerous specific details are set forth in order to provide a thorough understanding of the invention. However, it will be understood by those skilled in the art that the present invention may be practiced without these specific details. In other instances, well-known methods, procedures, and components have not been described in detail so as not to obscure the present invention.

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[0019] Embodiments of the invention are directed to formulations comprising Strontium and Methylsulfonylmethane (MSM). The combination of Strontium and Methylsulfonylmethane (MSM) may be referred to in the application as “the combination”.

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[0020] Further embodiments of the invention are directed to methods of treating or preventing stinging, itching, burning, erythema and other sensations and feelings, and their development, associated with skin irritant products, chemicals, processes and other reasons of irritation or such feelings, with change of temperatures, with burns or with change of pH, wherein the method comprises administering a formulation comprising Strontium and Methylsulfonylmethane (MSM).

[0021] The present invention relates to the surprising discovery that the combination of Strontium with Methylsulfonylmethane (MSM) in a topical product(s) formulation is useful in reducing the development, incidence and severity of irritation and erythema associated with topically applied skin irritants, including irritation and neurogenic inflammations caused by various ingredients of skin treatment products.

[0022] This effect of Strontium with Methylsulfonylmethane (MSM) is a synergistic effect. The synergistic effect is characterized by the combination of two materials having a stronger effect than the simple sum of the effect of each material. This is further illustrated in the example section below and in tables 1 and 2.

[0023] The synergistic effect also enables the use of small amounts of Strontium and MSM which are not effective or have a very low effect on their own.

[0024] The present invention enables using high concentration of active cosmetic ingredients in cosmetic products, usually with a low pH, without the typical irritations and side effects (redness etc.) resulting from the chemical irritant or the low pH, by adding Strontium and MSM to the cosmetic product formula.

[0025] The combination of Strontium and MSM can be used in a formulation and/or product comprising an active cosmetic ingredient, or used prior or post the use of a topical cosmetic product or prior or post performing a treatment to the skin (for example, laser treatment or other treatments) or post sun exposure or post burns. When the combination is not part of the product and is applied before or after the product or treatment or sun exposure, the combination should be used in close proximity timewise in order to have the desired effect of reducing irritation and erythema.

[0026] This invention enables more efficacious products for the treatment of the skin, without the typical side effects: redness, itching, burning, stinging, etc. The effectiveness of the products is increased because the subject is more likely to use the product as prescribed if there are no side effects or the side effects are mild. In addition, the aesthetician/doctor

administering/applying a treatment is more likely to keep the products on for longer if the customer/patient is not suffering or uncomfortable. For example, one can leave a chemical peel on the treated area for longer, if there is less irritation, and thus receive the full effectiveness that is embodied in the product. In addition, it enables the subject or the practitioner to increase the amount of active ingredient since the side effects of irritation and redness are eliminated or reduced.

[0027] In addition to reducing the side effects, the effectiveness of the active ingredient(s) is not harmed or compromised with the addition of Strontium and MSM.

[0028] In some embodiments, the combination can be used for alleviating irritation and erythema associated with skin diseases such as Atopic Dermatitis, Eczema, Seborrhea, Rosacea and Psoriasis.

[0029] In some embodiments, the combination can be used for treating dry skin as a result of environment conditions such as "winter itch".

[0030] In some embodiments, the combination is used in products for treating acne.

[0031] In some embodiments, the combination is used in products for anti-aging.

[0032] In some embodiments, the Strontium and MSM may be in separate products and are applied one after the other in order to achieve the desired effect of reducing irritation and erythema. In some embodiments, the Strontium is applied and immediately afterwards MSM is applied. In some embodiments, the MSM is applied and immediately afterwards Strontium is applied.

[0033] In some embodiments, the formulation further comprises one or more additional active cosmetic ingredient(s).

[0034] In some embodiments, the additional active cosmetic ingredient is Alpha Hydroxy Acid (AHA) (including Glycolic acid, Lactic acid, Mandelic acid, Tartaric acid, Malic acid and Citric acid), Beta Hydroxy Acid (BHA) (including Salicylic acid and Citric acid), Retinol, Alpha Keto Acids (such as Pyruvic Acid), Dicarboxylic Acids (such as Azelaic Acid), Arbutin (such as alpha and beta Arbutin) or Vitamin C.

[0035] In one embodiment, the active cosmetic ingredient is Azelaic Acid.

[0036] In one embodiment, the active cosmetic ingredient is Glycolic acid.

[0037] In some embodiments, the present invention relates to a combination of Strontium and MSM in a topical product which is effective as cosmetic treatment to the skin, and supports skin soothing and calmness of the skin during treatment, and overall calmness of

the skin, as well as providing a cosmetic effect to the skin, such as improving skin appearance. When topically applied to the skin, the combination improves the skin appearance.

[0038] Trials demonstrated that when the combination of Strontium and MSM is applied
5 topically to the skin it immediately and effectively prevents the sensations of stinging, itching, burning, erythema and other sensations and feelings associated with skin irritant products and with change of temperatures and with burns and with change of pH and with chemical irritants among others, such as for example high concentration AHA or BHA peel or products containing Retinols or Alpha Keto Acids (such as Pyruvic Acid) or Dicarboxylic
10 Acids (such as Azelaic Acid) or for example applying seawater to the skin after shaving.

[0039] Formulations containing the combination of Strontium and MSM are effective in preventing the development and suppressing the irritation associated with products, which contain components capable of causing irritation.

[0040] In some embodiments, when a combination of Strontium and
15 Methylsulfonylmethane (MSM) is applied topically to the skin, it is immediately, effectively and for long period of time prevents the sensations of stinging, itching, burning, erythema and other sensations and feelings associated with skin irritant chemicals and products and other types of neurogenic inflammations.

[0041] The combination is also effective for treating sensations and neurogenic
20 inflammation caused by chemicals, changes in temperature, burns among others, and from low pH, such as in AHA and BHA (Alpha/Beta Hydroxy Acid) peels and Retinols and Alpha Keto Acids (such as Pyruvic Acid) and Dicarboxylic Acids (such as Azelaic Acid) and other types of chemical peels and other types of medical and cosmetics products that cause topical irritations. The combination of Strontium and MSM significantly extends the duration of the
25 anti-irritation effect compared to each one on its own. The anti-irritant effect is immediate and in real-time, with no need to wait between the time of applying the composition and the time it starts to have an effect.

[0042] In some embodiments the concentration of elemental Strontium is in a range of 0.1
30 to 10 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 2-8 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 2-4 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 4-6 % w/w in the formulation. In some

embodiments the concentration of Strontium is in a range of 6-8 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 5-7 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 2-5 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 7-10 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 8-10 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 0.1-2 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 0.1-15 % w/w in the formulation. In some embodiments the concentration of Strontium is in a range of 10-15 % w/w in the formulation.

5 [0043] In some embodiments the concentration of Strontium is in a range of 0.1 to 10 % w/w in the formulation.

[0044] In some embodiments the concentration of Strontium is in a range of 2-8 % w/w in the formulation.

[0045] In some embodiments the concentration of MSM is in a range of 0.1 to 20 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 5-10 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 5-7 % w/w in the formulation. In some embodiments the concentration of MSM is 7-10 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 6-8 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 6-9 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 0.1-5 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 10-20 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 10-15 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 15-20 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 0.1-3 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 3-5 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 0.1 to 40 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 20-40 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 20-30 % w/w in the formulation. In some embodiments the concentration of MSM is in a range of 30-40 % w/w in the formulation.

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[0046] In some embodiments the concentration of MSM is in a range of 0.1 to 20 % w/w in the formulation.

[0047] In some embodiments the concentration of MSM is in a range of 5-10 % w/w in the formulation.

- 5 [0048] The higher the concentration of the cosmetic active ingredient a higher concentration of the combination of Strontium and MSM is recommended.

[0049] In some embodiments the counter anion for the Strontium cation is a halogen.

[0050] In some embodiments the halogen is fluoride (F⁻), chloride (Cl⁻), bromide (Br⁻) or iodide (I⁻).

- 10 [0051] In some embodiments the halogen is chloride.

[0052] In some embodiments the counter anion is organic such as carboxylic acids, alkoxylates, amino acids (especially, lysine, arginine, histidine, ornithine, aspartic acid, glutamic acid, proline, and cysteine), peptides, saturated and unsaturated organic acids, and saturated and unsaturated fatty acids.

- 15 [0053] In some embodiments, the organic counter anion is acetate, lactate, glycolate, tartrate, maleate, benzoate, propionate, salicylate, ascorbate, formate, succinate, folinate, aspartate, phthalate, oleate, palmitate, stearate, lauryl sulfate, lanolate, myristate, behenate, caseinate, cyclamate, pantothenate, EDTA or other polyaminopolycarboxylates, saccharin, thioglycolate, laurate, methylparaben, propylparaben, ricinoleate or sorbate anions.

- 20 [0054] In some embodiments the Strontium is in the form of Strontium Chloride, Strontium Acetate or Strontium Nitrate.

[0055] In some embodiments the Strontium is in the form of Strontium Chloride Hexahydrate.

- 25 [0056] In some embodiments the formulation further comprises a dermatologically acceptable carrier. A "dermatologically acceptable carrier" as used herein means a carrier is suitable for topical application to keratinous tissue, compatible with the actives in the formulation, that will not cause safety or toxicity concerns. Examples of dermatologically acceptable carriers are well known in the art and may comprise about 0.1 to 99.1 % of a cosmetic formulation.

- 30 [0057] In some embodiments the composition is administered in any pharmaceutical or cosmetic formulation that enables the administration to a skin tissue of a patient.

[0058] In some embodiments the composition or topical medicament of the present invention comprises a carrier. According to embodiments of the present invention the carrier is in the form of an ointment, a cream, a lotion, an oil, a solution (in some embodiments an aqueous solution), an emulsion, a gel, a paste, a milk, an aerosol, a powder, or a foam. In some embodiments the carrier is an aqueous-based carrier (such as a gel, oil-in water emulsion or oil-in water cream, aqueous solution, foam, lotion, spray).

[0059] In some embodiments the formulation is administered in products such as a mask, a peel, a soap (liquid or solid), a shampoo, a shaving cream, after shave, sunscreen, perfume, deodorant, anti-aging and anti-wrinkle, artificial tanning, makeup and makeup removers, baby products.

[0060] In some embodiments the formulation is in the form of a topical oral formulation. In some embodiments the formulation is administered in products such as mouthwash or lozenges. A physiologically acceptable carrier for topical administration as used herein includes the dermatologically acceptable carriers defined above, and carriers adapted for topical administration in the mouth.

[0061] Typical modes of application of the formulation/product include fingers, a physical applicator such as a brush, as stick, swab, tissue or cloth, or by applying or adhering a prepared applicator already containing the formulation such as a cloth mask.

[0062] In some embodiments the formulations may further comprise one or more of the following: emulsifiers, solvents, surfactants, preservatives, moisturizer, fragrances, dyes/colorants, viscosity adjustment agents, emollients, binders, absorbents, buffering agents, chelating agents, conditioning agents

[0063] The formulations of the present invention all preserve the primary activity of the topical product while allowing the anti-irritation and anti-erythema activity of the formulation to provide patient benefit.

Examples**Example I - Glycolic Acid 50% (pH 0.9)**

[0064] A cosmetic peel comprising Glycolic Acid 50% (pH 0.9) was administered to 15 volunteers, between the ages 23 to 64 years (Average 45). The peel was kept on the treated area for 10 minutes. Erythema and irritation (itching, stinging and burning) were evaluated before applying the product and 10 minutes after applying the product.

[0065] The peel further comprised one of the following combinations of Strontium Chloride and MSM:

- No addition of Strontium Chloride and no addition of MSM;
- 10% MSM only;
- 5% Strontium Chloride only (which equals about 2.75% of elemental Strontium); or
- 5% Strontium Chloride + 10% MSM.

[0066] Different types of skin tone (Fitzpatrick) and conditions (oily, regular, etc.) participated in the trials.

[0067] Erythema was evaluated using a colorimeter device that provides values using CIE-L*a*b* Coordinates.

[0068] Irritation was evaluated using standardized Visual Analogue Scale (VAS) of 0 to 10.

[0069] The results are presented below in table 1, wherein Delta a* is the difference in redness between the measurement before the peel and 10 minutes after the peel and Delta E* is difference in overall skin tone between the measurement before the peel and 10 minutes after the peel.

[0070] The first row in the table is the "base" row wherein the cosmetic peel was administered without Strontium and/or MSM. The last three columns in the table compare the change in Delta a*, Delta E* and irritation compared to the base line. For example, for the second row where 10% MSM was administered the Delta a* is 5.62 (an average for the participating subjects) which is 6.53% lower than the Delta a* of the base row as noted in column 4.

Table 1:

Formula	Delta a*	Delta E*	Irritation	Delta a* % from base	Delta E* % from base	Delta Irritation % from base
0% Str , 0% MSM	6.02	8.87	8.07			
0% Str , 10% MSM	5.62	8.36	7.73	-6.53%	-5.73%	-4.13%
5% Str , 0% MSM	5.44	7.99	6.93	-9.57%	-9.95%	-14.05%
5% Str , 10% MSM	3.47	5.21	3.53	-42.33%	-41.27%	-56.2%

[0071] The synergistic effect of the combination can be clearly seen from the results in Table 1. The Delta a* of 10% MSM on its own is 5.62 and the reduction compared to the base is 6.53%, the Delta a* of 5% Strontium Chloride on its own is 5.44 and the reduction compared to the base is 9.57%, while the Delta a* of the combination of 10% MSM and 5% Strontium Chloride is 3.47 which is a 42.33% reduction compared to the base. This reduction is more than the sum of each of the reductions on their own and accordingly demonstrates the synergistic effect.

[0072] The effect of the combination is also illustrated in the figures and described below.

[0073] Fig. 1 depicts comparative clinical data from Example I showing an effect on skin redness (delta a*) with formulations according to the invention. Delta a*% represents the percent of increase in redness of the skin after applying the peel compared to the color before. The graph indicates this change for each of the 15 volunteers. As can be seen, the top three graph lines, which include the following three combination: no addition of Strontium Chloride and no addition of MSM; 10% MSM only and 5% Strontium Chloride only, show an increase of about 30-35% in redness while the combination of 5% Strontium Chloride and 10% MSM shows an increase on average of only about 20%.

[0074] Fig. 2 depicts comparative clinical data from Example I showing an effect on overall skin color (delta E*) with formulations according to the invention. Delta E* represents the

difference in overall skin tone between the measurement before the peel and after the peel. The graph indicates this change for each of the 15 volunteers. As can be seen, the overall skin tone change for the combination of 5% Strontium Chloride and 10% MSM was lower than the other three combinations.

5 [0075] Fig. 3 depicts comparative clinical data from Example I showing an effect on skin irritation level with formulations according to the invention. The graph indicates the irritation level for each of the 15 volunteers, measured 10 minutes after applying the peel. As can be seen the irritation level for the combination of 5% Strontium Chloride and 10% MSM was lower than the level for the other three combinations.

10 [0076] Fig. 4 depicts a comparison of the data shown in Table 1, columns 1-3, and demonstrating the lower values, in all three parameters of Delta a*, Delta E* and irritation, of the combination of 5% Strontium Chloride and 10% compared to the other three combinations.

[0077] Fig. 5 depicts a comparison of improvement-from-baseline (no addition of Strontium Chloride and no addition of MSM) of the data shown in Table 1, columns 4-6, and demonstrating the higher reduction percentages compared to the base line, in all three parameters of Delta a*, Delta E* and irritation, of the combination of 5% Strontium Chloride and 10% compared to the other two combinations.

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Example II - Azelaic Acid 25% (pH 3.5)

[0078] A cosmetic product comprising Azelaic Acid 25% (pH 3.5) was administered to 15 volunteers, between the ages 23 to 64 years (Average 45). Erythema and irritation (itching, stinging and burning) were evaluated before applying the product and 10 minutes after
25 applying the product.

[0079] The product further comprised one of the following combinations of Strontium Chloride and MSM:

- No addition of Strontium Chloride and no addition of MSM;
- 30 - 10% MSM only;
- 5% Strontium Chloride only (which equals about 2.75% of elemental Strontium); or
- 5% Strontium Chloride + 10% MSM.

[0080] Different types of skin tone (Fitzpatrick) and condition (oily, regular, etc.) participated in the trials.

[0081] Erythema was evaluated using a colorimeter device that provides values using CIE-
5 L*a*b* Coordinates.

[0082] Irritation was evaluated using standardized Visual Analogue Scale (VAS) of 0 to 10.

[0083] The results are presented below in table 2, wherein Delta a* is the difference in redness between the measurement before applying the product and 10 minutes after the
10 applying the product and Delta E* is difference in overall skin tone between the measurement before applying the product and 10 minutes after applying the product.

The first row in the table is the “base” row wherein the cosmetic product was administered without Strontium and/or MSM. The last three columns in the table compare the change in Delta a*, Delta E* and irritation compared to the base line. For example, for the second
15 row where 10% MSM was administered the Delta a* is 4.35 which is 3.77% lower than the Delta a* of the base row, as noted in column 4.

Table 2:

Formula	Delta a*	Delta E*	Irritation	Delta a* % from base	Delta E* % from base	Delta Irritation % from base
0% Str , 0% MSM	4.52	6.35	5.6			
0% Str , 10% MSM	4.35	6.08	4.87	-3.77%	-4.27%	-13.10%
5% Str , 0% MSM	4.12	5.73	4.73	-8.83%	-9.72%	-15.48%
5% Str , 10% MSM	2.6	3.71	2.4	-42.47%	-41.57%	-57.14%

[0084] The synergistic effect of the combination can be clearly seen from the results in Table 2. The Delta a^* of 10% MSM on its own is 4.35 and the reduction compared to the base is 3.77%, the Delta a^* of 5% Strontium on its own is 4.12 and the reduction compared to the base is 8.83%, while the Delta a^* of the combination of 10% MSM and 5% Strontium is 2.6 which is a 42.47% reduction compared to the base. This reduction is more than the sum of each of the reductions on their own and accordingly demonstrates the synergistic effect.

[0085] The effect of the combination is also illustrated in the figures.

[0086] Fig. 6 depicts comparative clinical data from Example II showing an effect on skin redness (delta a^*) with formulations according to the invention. Delta $a^*%$ represents the percent of increase in redness of the skin after applying the product compared to the color before. The graph indicates this change for each of the 15 volunteers. As can be seen, the top three graph lines, which include the following three combination: no addition of Strontium Chloride and no addition of MSM; 10% MSM only and 5% Strontium Chloride only, show an increase of about 20-25% in redness while the combination of 5% Strontium Chloride and 10% MSM shows an increase on average of only about 10-15%.

[0087] Fig. 7 depicts comparative clinical data from Example II showing an effect on overall skin color (delta E^*) with formulations according to the invention. Delta E^* represents the difference in overall skin tone between the measurement before the product and after the product. The graph indicates this change for each of the 15 volunteers. As can be seen, the overall skin tone change for the combination of 5% Strontium Chloride and 10% MSM was lower than the other three combinations.

[0088] Fig. 8 depicts comparative clinical data from Example II showing an effect on skin irritation level with formulations according to the invention. The graph indicates the irritation level for each of the 15 volunteers, measured 10 minutes after applying the product. As can be seen the irritation level for the combination of 5% Strontium Chloride and 10% MSM was lower than the level for the other three combinations.

[0089] Fig. 9 depicts a comparison of the data shown in Table 2, columns 1-3, and demonstrating the lower values, in all three parameters of Delta a^* , Delta E^* and irritation, of the combination of 5% Strontium Chloride and 10% compared to the other three combinations.

[0090] Fig. 10 depicts a comparison of improvement-from-baseline (no addition of Strontium Chloride and no addition of MSM) of the data shown in Table 2, columns 4-6, and demonstrating the higher reduction percentages compared to the base line, in all three
5 parameters of Delta a*, Delta E* and irritation, of the combination of 5% Strontium Chloride and 10% compared to the other two combinations.

[0091] While certain features of the invention have been illustrated and described herein, many modifications, substitutions, changes, and equivalents will now occur to those of
10 ordinary skill in the art. It is, therefore, to be understood that the appended claims are intended to cover all such modifications and changes as fall within the true spirit of the invention.