

Medical Education Article

Impact of Consciousness Energy Healing Treatment on the Telogen Skin of Hair Follicles of C57BL/6 Mice

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Development of hair follicle is undergoing cycles of three phases like anagen, catagen, and telogen. Adequate hair growth is essential for social interaction and outlook in human life. In this context, the present study was performed for the assessment of the impact of Biofield Energy Healing (The Trivedi Effect[®]) Treatment on the test item (1:1 ratio mixture of herbal extracts of *Phyllanthus emblica* and *Eclipta alba*) in C57BL/6 mice. The test item was divided into two parts. One part was denoted as the untreated and test item without any Biofield Energy Treatment, while the other part was defined as the Biofield Energy Treated test item, which received the Consciousness Energy Healing Treatment by a renowned Biofield Energy Healer, Alice Branton. The study parameters like anagen induction and visual melanogenesis using skin biopsy technique were used in this experiment for the assessment of hair growth phases. The experimental results of the untreated and Biofield Energy Treated test item groups showed 50% and 60%, respectively of hair growth on dorsal clipped skin after topical application compared to the vehicle control group. Besides, the Biofield Energy Treated test item exhibited 60% melanogenesis after biopsy analysis in mice skin at the end of experiment compared with the vehicle control group. The overall results demonstrated that the Biofield Energy Treatment has the potential for hair growth promotion as evident *via* increased hair growth and melanogenesis. Therefore, the Biofield Energy Healing (The Trivedi Effect[®]) Treatment could be useful as a hair growth promoter for various treatment of skin injuries and skin-related disorders like necrotizing fasciitis, actinic keratosis, sebaceous cysts, diaper rash, decubitus ulcer, etc.

Keywords: Biofield Energy Healing, Consciousness Energy Healing Treatment, The Trivedi Effect[®], Telogen skin, Melanogenesis, Skin health

1. INTRODUCTION

Growth of complete hair follicles occurs through three different phases such as anagen, catagen, and telogen (Hardy 1992; Paus and Cotsarelis 1999; Stenn et al. 1996). Most common disorder related to hair growth is alopecia (Gordon and Tosti 2011; Alsantali 2011). Apart from this, androgenetic alopecia (AGA) or also called as male pattern baldness, is a form of hair loss that occurs in both males and females. However, the probable mechanism is due to synthesis, metabolism, and signaling of androgen which mediated through the androgen receptor (Crabtree et al. 2010). Numerous literature reported some disadvantages of *in vitro* hair follicle growth model compared to animal

models (Matsuzaki and Yoshizato 1998). However, *in vivo* model minimize and reduce the demerits of hair follicle growth and extensively utilized most of the researcher (Kondo et al. 1990; Chase et al. 1951; Paus et al. 1989). Hence, based on the adequate and better results in *in vivo* study rather than *in vitro* experiment, authors designed this experiment and male mice was selected as the test system. From literature reported that minoxidil is widely used to treat hair loss without any severe adverse effects (Vesoulis et al. 2014), hence minoxidil was chosen as reference standard in this experiment for the assessment of hair growth. It also promotes hair growth *via* the stimulation of growth factor

release from adipose-derived stem cells dermal papilla and epithelial cells (Choi et al. 2018). Recently, natural products and plant extracts that are reported to promote a significant hair growth have been widely used in the hair care industry (Dhanotia et al. 2011). In recent years, several scientific reports and clinical trials have revealed the useful effects of Biofield Energy Treatment, which have shown to enhance the immune function in cases of cervical cancer patients *via* therapeutic touch (Lutgendorf et al. 2010) massage therapy (Ironson et al. 1996) etc. Complementary and Alternative Medicine (CAM) therapies are now rising as preferred models of treatment, among which Biofield Therapy (or Healing Modalities) is one approach that has been reported to have several benefits to enhance physical, mental and emotional human wellness. However, as per the data of 2012 from the National Health Interview Survey (NHIS), which indicated that the highest percentage (17.7%) of the Americans used dietary supplements as a complementary health approach as compared with other practices in past years. The National Center of Complementary and Integrative Health (NCCIH) has recognized and accepted Biofield Energy Healing as a CAM health care approach in addition to other therapies, medicines and practices such as natural products, deep breathing, yoga, Tai Chi, Qi Gong, chiropractic/osteopathic manipulation, meditation, massage, special diets, homeopathy, progressive relaxation, guided imagery, acupressure, acupuncture, relaxation techniques, hypnotherapy, healing touch, movement therapy, pilates, rolfing structural integration, mindfulness, Ayurvedic medicine, traditional Chinese herbs and medicines, naturopathy, essential oils, aromatherapy, Reiki, and cranial sacral therapy. Human Biofield Energy has subtle energy that has the capacity to work in an effective manner (Jain et al. 2015). CAM therapies have been practiced worldwide with reported clinical benefits in different health disease profiles (Rubik 2002). This energy can be harnessed and transmitted by the experts into living and non-living things *via* the process of Biofield Energy Healing. Biofield Energy Treatment (The Trivedi Effect[®]) has been published in numerous peer-reviewed science journals with significant outcomes in many scientific fields such as cancer research (Trivedi et al. 2015a,b), microbiology (Trivedi et al. 2015c,d,e,f), biotechnology (Trivedi et al. 2015g,h), pharmaceutical science (Trivedi et al. i,j,k,l), agricultural science (Trivedi et al. m,n,o,p), materials science (Trivedi et al. q,r,s,t), nutraceuticals (Trivedi et al. 2015u,v), skin health, human health and wellness.

Based on the literature information and importance of Biofield Energy Healing Treatment on various fields, the authors sought to evaluate the impact of the Biofield Energy Treatment (The Trivedi Effect[®]) on the test item (the 1:1 mixture of herbal extracts of

Phyllanthus emblica and *Eclipta alba*) for hair cells growth activity with respect to the assessment of different hair growth parameters like anagen induction in terms of hair growth score and melanogenesis using standard biopsy assay in male C57BL/6 mice.

2. MATERIALS AND METHODS

2.1. Chemicals and Reagents

The positive control, minoxidil sulphate was purchased from Dr. Reddy's Laboratories Ltd, India. The 1:1 ratio of herbal extracts of *Phyllanthus emblica* and *Eclipta alba* were obtained from M/s. Sanat Products Ltd., India. All the other chemicals used in this experiment were analytical grade procured from India.

2.2. Experimental Animals

Randomly breed male C57BL/6 mice body weight ranges between 22 to 24 gm were used in this experiment. The animals were purchased from M/s. Vivo Bio Tech Ltd., Hyderabad, India. Animals were randomly divided into four groups based on their body weights consist of total eighteen animals. They were kept individually in sterilized polypropylene cages with stainless steel top grill having provision for holding pellet feed and drinking water bottle fitted with stainless steel sipper tube. The test facility is registered for breeding and experiment of animals with the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Ministry of Environment and Forest, Govt. of India. Study was approved by Institutional Animal Ethics Committee and the husbandry conditions was maintained as per CPCSEA recommendations (IAEC No.: IAEC/41/502). All the procedures and protocols related to animal experiment were approved and followed by institutional animal ethics committee (IAEC). All the animals were housed under standard experimental conditions, with room temperature ($22 \pm 3^\circ\text{C}$), relative humidity (30% to 70%).

2.3. Experimental Design

Animals were grouped into following treatment groups. Group 1 was served as vehicle control (Poly ethylene glycol: Ethyl alcohol). Group 2 was defined as positive control (minoxidil sulphate). Group 3 was defined as the untreated test item (mixture of herbal extracts) and group 4 defined as the Biofield Energy Treated test item (mixture of herbal extracts). The dose regime for test item treated group was thrice daily application for

total of 28 days, while for positive control and vehicle group, the regimen was twice daily application for total of 22 and 28 days, respectively.

2.4. Biofield Energy Healing Approach

The test item (a 1:1 mixture of herbal extracts of *Phyllanthus emblica* and *Eclipta alba*) was used in this experiment for the assessment of hair growth in male C57BL/6 mice. The test item was divided into two parts. One part was considered as control, where no Biofield Energy Treatment was given. Further, the control group was treated with “sham” healer for better comparison purpose. The sham healer did not have any knowledge about the Biofield Energy Healing Treatment. Second part of the test item was received Biofield Energy Healing Treatment (known as The Trivedi Effect®) under laboratory conditions for 3 minutes through the Alice Branton’s unique Biofield Energy Transmission process to the test item. Biofield Energy Healer in this study did not visit the laboratory, nor had any contact with the test samples. After that, the Biofield Energy Treated and untreated test items were kept in similar sealed conditions and used for the study as per the study plan.

2.5. Clipping of Animals

The telogen skin look visually as pink skin of the test animals was exposed by gentle clipping of hair from the dorsal back (approx. 4X4cm²) using an electrical clipper one day before the application with the test item/positive control/vehicle.

2.6. Body Weight

Body weight of each animal was noted before the application of test item or positive control to the animals and then once a week throughout the study.

2.7. Visual Melanogenesis

The animals in each group were observed by visual examination of the color of the area of dorsal skin of the animal. The skin color change was scored on a scale of 0-3 based upon the visual observations. The criterion of scoring the hair growth of animals is described in Table 1.

Table 1: Scoring of hair growth and criteria for grading.

S. No.	Observation	Hair growth score
1	No hair growth, pink skin	0
2	Skin color changes from pink to gray/light gray without visible hair growth	0.5
3	Skin color changes from gray/light grey to dark gray/black without visible hair growth, indicating the onset of anagen	1
4	Sparse hair growth	1.5
5	Diffuse short hair growth	2
6	Moderate hair growth	2.5
7	Dense, normal coat hair	3

2.8. Statistical Analysis

Data were represented as mean \pm standard error of mean (SEM) and also as percentage of the respective parameters. For statistical analysis Sigma-

Plot (version 11.0) was used as a statistical tool. Statistically significant values were set at the level of $p \leq 0.05$.

3. RESULTS AND DISCUSSION

3.1. General Health Status

During the course of the study, there were no signs of behavioral changes, reaction to treatment or ill health observed in all the animals treated with test item.

3.2. Body Weight

Treatment with the test item did not show to any adverse effects on body weight in any of the animals

during the study *i.e.*, body weight was gain on normal basis as like vehicle control group (Data not shown).

3.3. Anagen Induction and Hair Growth

The vehicle control group did not show any anagen induction or hair growth in any of the animal. The mean hair growth score of the untreated and Biofield Energy Treated test item groups are shown in Figure 1.

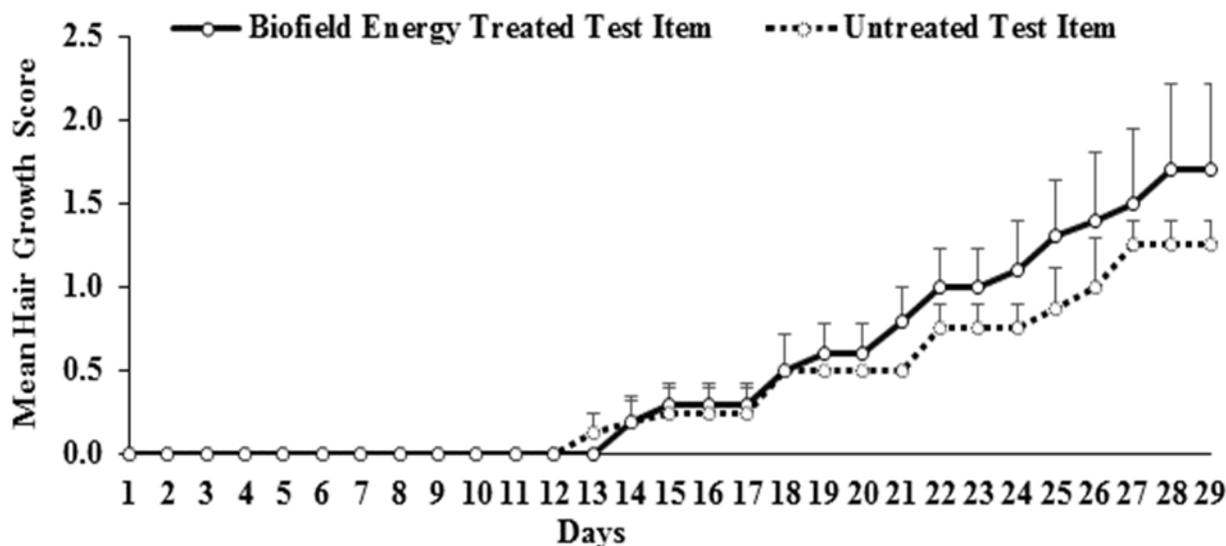


Figure 1: Evaluation of mean hair growth score of the untreated and Biofield Energy Treated test item (1:1 mixture of herbal extracts of *Phyllanthus emblica* and *Eclipta alba*) in male C57BL/6 mice.

The positive control, minoxidil sulphate led to anagen induction followed by hair growth in four animals out of four *i.e.*, 100%. The results showed that the untreated test item showed a visual anagen induction on dorsal clipped of skin in four animals out of four followed by hair growth in two animals out of four *i.e.*, 50% after topical application. Moreover, the Biofield Energy Treated test item showed a visual anagen induction on dorsal clipped of skin followed by hair growth after topical application in three mice out of five *i.e.*, 60%. From Figure 1, it was stated that the Biofield Energy Treated test item group started early of hair growth (on day 9) compared to the untreated test item group (on day 12). The principal function of hair follicles is for the production of hair (Hardy 1992; Wessells and Roessner 1965). The hair follicle, so called as a specific mini-organ of the skin, is composed of epidermal (epithelial) and dermal

(mesenchymal) compartments, and their interaction also plays an important role for the growth of hair follicle (Millar 2002; Cotsarelis 2006). Female pattern hair loss is the most common disorder associated with hair shedding and it is more prevalent in older aged peoples (Gan and Sinclair 2005).

Like this, many more pathological condition promotion of hair growth is necessary. In this context, authors performed this experiment to see the effect of Biofield Energy Treatment on hair follicles growth and development. Overall, there was an improvement of hair follicle growth in the Biofield Energy Treated test item group as compared to the untreated test item group, which might be due to the effect of Consciousness Energy Healing Treatment by renowned Biofield Energy Healer (The Trivedi Effect®).

3.4. Visual Melanogenesis by Skin Biopsy

The results of melanogenesis after skin biopsy were recorded in the peeled skin of all the groups are shown in Figure 2. No visual melanogenesis was recorded in the peeled skin of animals treated with the vehicle. However, in the positive control group (minoxidil sulphate) showed 100% melanogenesis in the peeled

skin of four animals out of four animals *i.e.*, 100%. Moreover, the untreated and Biofield Energy Treated test item exhibited 100% and 60% melanogenesis, respectively after treatment with the 1:1 mixture of herbal extracts of *Phyllanthus emblica* and *Eclipta alba* in mice (Figure 2).

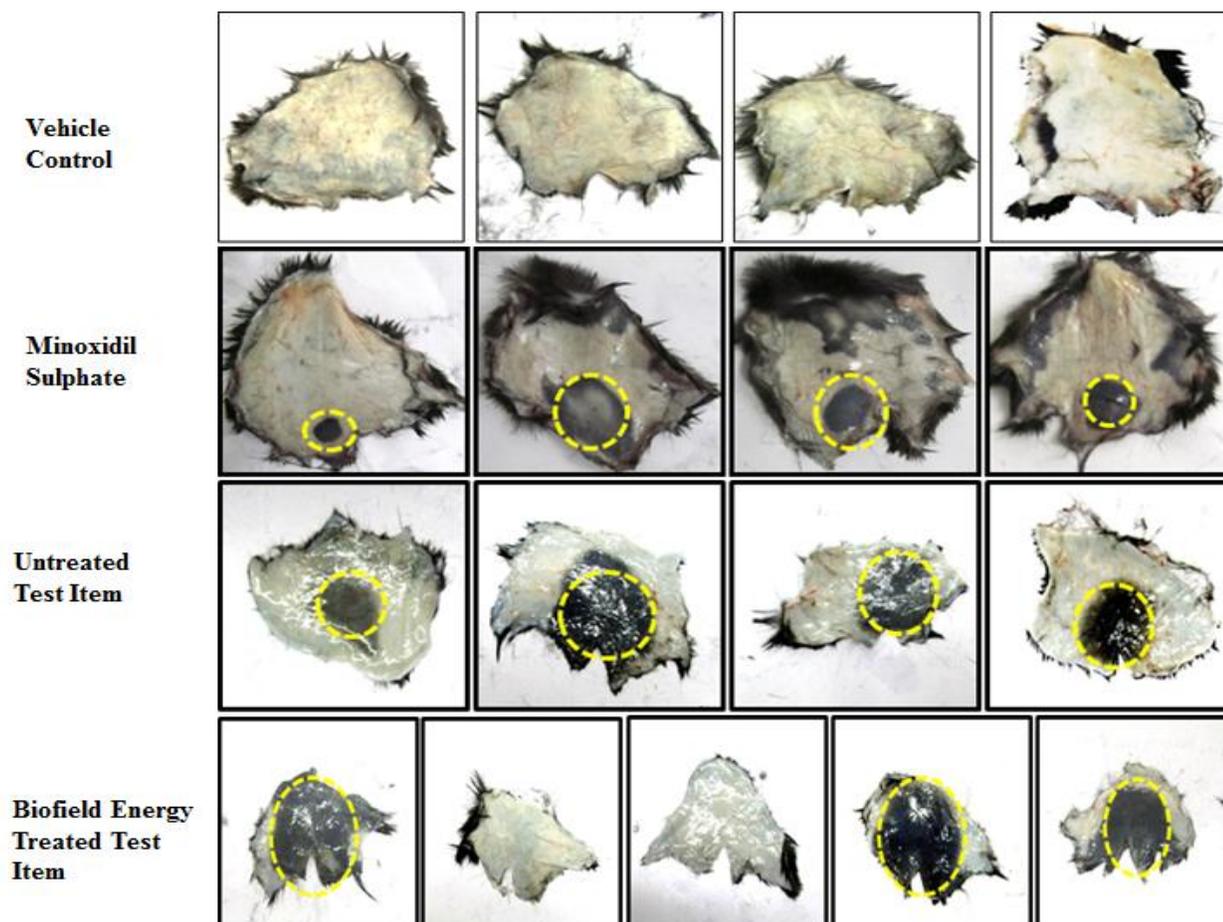


Figure 2: Representative biopsy photomicrograph of the various treatment groups showing hair growth at the end of experiment in mice.

Overall, the Biofield Energy Treated test item remarkably improved hair growth. Based on that, it is assumed that in this experiment the improvement of hair cell growth and development could be due to the impact of The Trivedi Effect® - Biofield Energy Healing Treatment.

4. CONCLUSIONS

Based on the study outcomes described the *in vivo* hair growth promotion activity of the Biofield Energy

Treated test item using C57BL/6 mice. Animals were topically treated with the test item, positive control and vehicle. The present study revealed that the application of Biofield Energy Treated test item in C57BL/6 mice led to faster anagen induction and faster rate of hair growth in 3/5 (60%) the animals. Whereas, the animal treated with untreated test item led to anagen induction followed by hair growth in 2/4 (50%) animals at a slower rate compared to the Biofield Energy Treated group. Further, the Biofield Energy Treated test item exhibited 60% melanogenesis after biopsy analysis compared to the untreated test item group. Hence, based on the current

study it can be concluded that treatment with Biofield Energy led to faster anagen induction and faster hair growth promotion efficacy as compared to the untreated test item group. In conclusion, The Trivedi Effect® - Consciousness Energy Healing Treatment might act as an effective hair growth enhancer and it can be used as a complementary and alternative treatment for the prevention of various types of skin-related disorders viz. necrotizing fasciitis, actinic keratosis, sebaceous cysts, diaper rash, decubitus ulcer, etc. Besides, it might be useful to improve cell-to-cell communication, normal cell growth, cell differentiation, neurotransmission, cell cycling and proliferation, hormonal balance, skin health, immune and cardiovascular functions. Besides, it can also be utilized in organ transplants (for example kidney transplants, liver transplants and heart transplants), hormonal imbalance, aging, and various immune related disease conditions such as Ulcerative Colitis, Alzheimer's Disease, Dermatitis, Irritable Bowel Syndrome, Asthma, Hashimoto Thyroiditis, Pernicious Anemia, Sjogren Syndrome, Multiple Sclerosis, Aplastic Anemia, Hepatitis, Diverticulitis, Graves' Disease, Dermatomyositis, Diabetes, Myasthenia Gravis, Parkinson's Disease, Atherosclerosis, Systemic Lupus Erythematosus, stress, etc. with a safe therapeutic index to improve overall health, and Quality of Life.

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REFERENCES

Alsantali A (2011) Alopecia areata: A new treatment plan. *ClinCosmetInvestig Dermatol* 4: 107-115.

^aTrivedi MK, Patil S, Shettigar H, Mondal SC, Jana S (2015) The potential impact of biofield treatment on human brain tumor cells: A time-lapse video microscopy. *J Integr Oncol* 4: 141.

^bTrivedi MK, Patil S, Shettigar H, Gangwar M, Jana S (2015) *In vitro* evaluation of biofield treatment on cancer biomarkers involved in endometrial and prostate cancer cell lines. *J Cancer Sci Ther* 7: 253-257.

Chase HB, Rauch H, Smith VW (1951) Critical stages of hair development and pigmentation in the mouse. *PhysiolZoöl* 24: 1-8.

Choi N, Shin S, Song SU, Sung JH (2018) Minoxidil promotes hair growth through stimulation of

growth factor release from adipose-derived stem cells. *Int J Mol Sci* 19: 691.

Cotsarelis G (2006) Epithelial stem cells: A folliculocentric view. *J Invest Dermatol* 126: 1459-1468.

Crabtree JS, Kilbourne EJ, Peano BJ, Chippari S, Kenney T, McNally C, Wang W, Harris HA, Winneker RC, Nagpal S, Thompson CC (2010) A mouse model of androgenetic alopecia. *Endocrinology* 151: 2373-2380.

^cTrivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) AntibioGram, biochemical reactions and biotyping of biofield treated *Providencia rettgeri*. *American Journal of Health Research* 3: 344-351.

Dhanotia R, Chauhan NS, Saraf DK, Dixit VK (2011) Effect of *Citrullus colocynthis* Schrad fruits on testosterone-induced alopecia. *Nat Prod Res* 25: 1432±43.

^dTrivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) Antimicrobial sensitivity, biochemical characteristics and biotyping of *Staphylococcus saprophyticus*: An impact of biofield energy treatment. *J Women's Health Care* 4: 271.

^eTrivedi MK, Branton A, Trivedi D, Nayak G, Shettigar H, Mondal SC, Jana S (2015) Antimicrobial susceptibility pattern, biochemical characteristics and biotyping of *Salmonella paratyphi A*: An impact of biofield treatment. *ClinMicrobiol* 4: 215.

^fTrivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) AntibioGram of biofield-treated *Shigella boydii*: Global burden of infections. *Science Journal of Clinical Medicine* 4: 121-126.

Gan DC, Sinclair RD J (2005) Prevalence of male and female pattern hair loss in Maryborough. *Investig Dermatol Symp Proc* 10: 184-189.

Gordon KA, Tosti A (2011) Alopecia: Evaluation and treatment. *Clin Cosmet Investig Dermatol* 4: 101-106.

Hardy MH (1992) The secret life of the hair follicle. *Trends Genet* 8: 55-61.

Ironson G, Field T, Scafidi F, Hashimoto M, Kumar M, Kumar A, Price A, Goncalves A, Burman I, Tetenman C, Patarca R, Fletcher MA (1996) Massage therapy is associated with enhancement of the immune system's cytotoxic capacity. *Int J Neurosci* 84: 205-217.

ⁱTrivedi MK, Patil S, Shettigar H, Bairwa K, Jana S (2015) Spectroscopic characterization of chloramphenicol and tetracycline: An impact of biofield. *Pharm Anal Acta* 6: 395.

Jain S, Hammerschlag R, Mills P, Cohen L, Krieger R, Vieten C, Lutgendorf S (2015) Clinical studies of biofield therapies: Summary, methodological

- challenges, and recommendations. *Glob Adv Health Med* 4: 58-66.
- [†]Trivedi MK, Patil S, Shettigar H, Bairwa K, Jana S (2015) Spectroscopic characterization of biofield treated metronidazole and tinidazole. *Med Chem* 5: 340-344.
- Kondo S, Hozumi Y, Aso K (1990) Organ culture of human scalp hair follicles: Effect of testosterone and oestrogen on hair growth. *Arch Dermatol Res* 282: 442-445.
- ^kTrivedi MK, Patil S, Shettigar H, Bairwa K, Jana S (2015) Effect of biofield treatment on spectral properties of paracetamol and piroxicam. *Chem Sci J* 6: 98.
- [†]Trivedi MK, Branton A, Trivedi D, Shettigar H, Bairwa K, Jana S (2015) Fourier transform infrared and ultraviolet-visible spectroscopic characterization of biofield treated salicylic acid and sparfloxacin. *Nat Prod Chem Res* 3: 186.
- Lutgendorf SK, Mullen-Houser E, Russell D, Degeest K, Jacobson G, Hart L, Bender D, Anderson B, Buekers TE, Goodheart MJ, Antoni MH, Sood AK, Lubaroff DM (2010) Preservation of immune function in cervical cancer patients during chemoradiation using a novel integrative approach. *Brain Behav and Immun* 24: 1231-1240.
- Matsuzaki T, Yoshizato K (1998) Role of hair papilla cells on induction and regeneration processes of hair follicles. *Wound Repair Regen* 6: 524-530.
- Millar SE (2002) Molecular mechanisms regulating hair follicle development. *J Invest Dermatol* 118: 216-225.
- ^mTrivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) Impact of biofield energy treatment on soil fertility. *Earth Sciences* 4: 275-279.
- ⁿTrivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) Evaluation of biochemical marker - Glutathione and DNA fingerprinting of biofield energy treated *Oryza sativa*. *American Journal of BioScience*. 3: 243-248.
- ^oTrivedi MK, Branton A, Trivedi D, Nayak G, Gangwar M, Jana S (2016) Molecular analysis of biofield treated eggplant and watermelon crops. *Adv Crop Sci Tech* 4: 208.
- Paus R, Cotsarelis G (1999) The biology of hair follicles. *N Engl J Med* 341: 491-497.
- Paus R, Stenn KS, Link RE (1989) The induction of anagen hair growth in telogen mouse skin by cyclosporine A. *Administration Lab Invest* 60: 365-369.
- ^pTrivedi MK, Branton A, Trivedi D, Nayak G, Gangwar M, Jana S (2015) Effect of biofield energy treatment on chlorophyll content, pathological study, and molecular analysis of cashew plant (*Anacardium occidentale* L.). *Journal of Plant Sciences* 3: 372-382.
- ^qTrivedi MK, Tallapragada RM, Branton A, Trivedi D, Nayak G, Latiyal O, Jana S (2015) Evaluation of atomic, physical, and thermal properties of bismuth oxide powder: An impact of biofield energy treatment. *American Journal of Nano Research and Applications* 3: 94-98.
- [†]Trivedi MK, Patil S, Nayak G, Jana S, Latiyal O (2015) Influence of biofield treatment on physical, structural and spectral properties of boron nitride. *J Material Sci Eng* 4: 181.
- Rubik B (2002) The biofield hypothesis: Its biophysical basis and role in medicine. *J Altern Complement Med* 8: 703-717.
- Stenn KS, Combates NJ, Eilertsen KJ, Gordon JS, Pardinias JR, Parimoo S, Prouty SM (1996) Hair follicle growth controls. *Dermatol Clin* 14: 543-558.
- ^sTrivedi MK, Nayak G, Patil S, Tallapragada RM, Latiyal O, Jana S (2015) Characterization of physical and structural properties of brass powder after biofield treatment. *J Powder Metall Min* 4: 134.
- Trivedi MK, Branton A, Trivedi D, Nayak G, Charan S, Jana S (2015) Phenotyping and 16S rDNA analysis after biofield treatment on *Citrobacter braakii*: A urinary pathogen. *J Clin Med Genom* 3: 129.
- Trivedi MK, Branton A, Trivedi D, Nayak G, Mondal SC, Jana S (2015) Evaluation of antibiogram, genotype and phylogenetic analysis of biofield treated *Nocardia otitidis*. *BiolSyst Open Access* 4: 143.
- [†]Trivedi MK, Nayak G, Patil S, Tallapragada RM, Latiyal O, Jana S (2015) Evaluation of biofield treatment on physical and structural properties of bronze powder. *Adv AutomobEng* 4: 119.
- ^uTrivedi MK, Nayak G, Patil S, Tallapragada RM, Jana S, Mishra RK (2015) Bio-field treatment: An effective strategy to improve the quality of beef extract and meat infusion powder. *J Nutr Food Sci* 5: 389.
- Vesoulis ZA, Attarian SJ, Zeller B, Cole FS (2014) Minoxidil-associated anorexia in an infant with refractory hypertension. *Pharmacotherapy* 34: e341±e4.
- ^vTrivedi MK, Tallapragada RM, Branton A, Trivedi D, Nayak G, Mishra RK, Jana S (2015) Biofield treatment: A potential strategy for modification of physical and thermal properties of gluten hydrolysate and ipomoea macroelements. *J Nutr Food Sci* 5: 414.
- Wessells NK, Roessner KD (1965) Nonproliferation in dermal condensations of mouse vibrissae and pelage hairs. *Dev Biol* 12: 419-433.