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RESEARCH ARTICLE

EXTRACTION, FORMULATION, PHYTOCHEMICAL CHARACTERIZATION, TOXICITY STUDY AND EVALUATION OF ANALGESIC ACTIVITY OF HERBAL SPAGYRIC ESSENCE (ELECTROHOMEOPATHIC MEDICINE) WHITE ELECTRICITY

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ABSTRACT

Objective: This particular research emphasis on the formulation, characterization and in vivo evaluation of analgesic activity of herbal spagyric essence (Electrohomeopathic medicine) White Electricity (WE) in Wistar rats. No scientific report has been available until date of WE. Therefore the current analysis focuses to prove scientific study of herbal spagiryc essence of WE. ***Materials and Methods:*** The Electrohomeopathic medicine WE is formulated by extracting and blending of spagiryc essence of specified herbal plants. The phytochemical characterization is done with help of qualitative chemical tests. The acute toxicity study is done with referring OECD toxicity guideline 420. The Analgesic activity of Electrohomeopathic medicine WE was carried out by the Acetic acid writhing reflex method, Tail immersion method and Hot plate method with using albino rats of either sex. The percentage protection against abdominal writhing and the pain reaction time were used to assess the degree of analgesia which has been measured and compared to control groups. ***Results:*** It was found that the Electrohomeopathic medicine WE is safe and non toxic. The acute toxicity study confirms the safety of drugs. It exhibited an excellent analgesic activity. The phytochemical investigation confirms the presence of phytoconstituents which justify the above pharmacological activity of WE.A decreasing the percentage abdominal writhing and increased the pain reaction time period when compared to control groups confirmed the potent activity of WE. ***Conclusion:*** This research indicates that electrohomeopathic medicine WE are relatively safe and effective in reducing pains in different animal models. Thus WE possess significant analgesic properties.

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INTRODUCTION

There is specific research activities developed across the world on the use of plant medication over some decade of time. Ayurveda, Siddha, Unani, Chinese, Homeopathy, and other traditional or may be folklore medical systems provided sufficient data for the safe and effective use of herbal medicines. In 1865, a pioneer Italian Count Cesare Mattie developed a new system of medicine and entitled as Electrohomeoapathy. He embraced the abstraction from a Swiss priest Parcelsus who was famous for chemical medicine. Parcelsus employed the techniques of preparing the natural substances by different methods of extraction, distillation, fermentation, cohobation and the final mixture incorporating a blend of different ingredients with additional effect. The conviction of Count Mattie was that as the human being is complex and his disease can only be cured by the use of complex remedies. These complex remedies could bring back the normal function of distinct organs and biochemical constituents into its appropriate status. Count Cesare Mattie believed the principle of Electrohomeopathy is "Complexia Complexes Curantor" (1). Subsequently, esteemed persons like Krauss (1914), N. L. Sinha (1920), Gidden (1956) and many more constructively attain their effort to make this system of medicine popular.

In the Electrohomeopathy system of medicine, cohobation technique is used to make spagyric essences from 114 plants for the therapy of different ailments. (2. 3) C.C. Mattie administered all 114 plants in the distinct league lean on their remedial properties and labeled as Scrofolso, Canceroso, Angiotico, Fabrifugo, Vermifugo, Venereo, Limphatico, Pettorale and a series of Electricities named as Red Electricity, White Electricity, Green electricity, Blue electricity and Yellow electricity (4). White Electricity comprises blend of spagyric essence of 16 different plants. It is widely used by local practitioners to get relief from all kinds of pains. However, literature survey does not reveal any scientific report on characterization and analgesic activity of WE. So the present study is an attempt to evaluate the analgesic efficacy as well as characterization of WE.

MATERIAL AND METHODS

Plant materials: All 16 plants used to formulate WE were collected from Himalaya Herbs, Saharanpur, UTAR PRADESH. (Gst no – 09AAZPG7334C1ZF). The identification and authentication of plant taxonomy were performed at Centre of Biotechnology, SOA University, Bhubaneswar.

The plant parts were washed softly through tap water to eliminate undesirable dirt particles. Subsequently, samples were air-dried under shade.

Animals: Wistar albino rats weighing 150-200 gm of either sex were procured from the animal house of School of Pharmaceutical Sciences, Siksha 'O' Anusandhan Deemed to be University. All the animals were kept in polycarbonate cages at an ambient temperature of 25 ± 5 °C having a relative humidity i.e., 55-65 % and 12 hr light and dark cycle. They were feed with a free standard food diet and water . All the experimental procedures were conducted in the morning hours, as per the standard guidelines for the care of laboratory animals. The experimental design was approved by the Institutional Animal Ethical Committee (IAEC) of the School of Pharmaceutical Sciences, Siksha 'O' Anusandhan Deemed to be University, and Odisha, India. Registration No.1171/C/08/CPCSE.

Chemicals& Instruments: Diclofenac sodium from Astrazeneca was purchased from a local chemist. Digital Plythesmometer (Inco, Ambala, India), Hot plate (Shreeji) and Analsgesiometer (Inco) was used for the experimental work.

Extraction & Formulation procedure: The extraction is done by the process of cohobation with referring to the 'method 26 German Homeopathy Pharmacopeia.' The extraction was carried out separately for all 16 plants essential to prepare WE. Then the spagyric essence of individual plants are blended as per the prescribed formula laid by Dr. N.L.Sinha.(5) (Table-1)

Table 1. Name of the plant and quantity used to prepare WE

Sl. No	Components	Parts
1.	*Achilia millefolium*	10
2.	*Anthemis nobilis*	10
3.	*Petrosalinum sativum*	20
4.	*Arnica Montana*	40
5.	*Genesta scoparia*	10
6.	*Guaiacum officinale*	20
7.	*Taraxcum officinale*	10
8.	*Ruta graveolens*	20
9.	*Sanguisorba officinalis*	10
10.	*Sanguinaria Canadensis*	10
11.	*Taxus baccata*	10
12.	*Avena sativa*	10
13.	*Viscum album*	10
14.	*Agaricus muscarious*	05
15.	*Cimicifuga racemosa*	10
16.	*Menyanthes trifoalaita*	05

Qualitative phytochemical analysis: Phytochemical screening of WE was performed as per the method described previously to unveil the presence of alkaloids , glycosides, flavonoids, tannins, phenols, aminoacids, carbohydratesm saponns, steroids and terpenoids. (6). (Table-2).

Acute Oral Toxicity: An acute toxicity study was carried out using the method of Lokey.(6) Twenty five mice of either sexes were randomly selected into five mice each. (Group I-V), Groups I, II, III, IV, V and they were dosed with 100, 500, 1000, 2000, and 3000 mg/kg bodyweight respectively orally by gastric gavage. The animals were allowed to access for food and water freely. They were observed over a period of 24 hour for signs of toxicity and mortality and found that all animals were safe. They are further kept under observation for 14 days more and did not notice any causality. So 300mg/body wt. ($1/10^{th}$ of maximum dose)was selected for analgesic study.

Acetic Acid Writhing Reflex method: This study was carried out with following the methods described by Koster with partial modification. (7) Eighteen albino mice of either sexes were casually divided into three groups (n = 6) of six mice in each group. They were fasted for 12 hours and later treated as follows; Group I mice were given distilled water of 10ml/kg body wt. (negative control group). Group II mice were given Diclofenac sodium of 400mg/kg body wt. (Positive control group). Group III were given WE of 300 mg/ kg body wt. (Approximately 5 drops) by gastric gavage. 1 hour after administration of drug, glacial 1% acetic acid (10ml/kg) was given intraperitoneally to all the mice to induce pain which was characterized by abdomen constriction of writhes. The number of writhes observed in each mouse was counted for 30 minutes and recorded. The percentage protection against abdominal breathing was used to assess degree of analgesia and calculated using formula. (8,9)

$$\frac{Mean\ control - Mean\ treated\ group}{Mean\ control} \times 100$$

Tail immersion test: This study was carried out with following the method described by Bhupesh et.al with little modification (10). Fasted eighteen albino mice of either sexes were casually divided into three groups (n=6) of six mice in each group. All were fasted for 12 hours but provided clean drinking water . Before treatment, its reaction time was determined at 0, 15, 30, 60, 120 and 180 minutes intervals, The mean of these six determinations constituted the "initial reaction time " ie. Reaction time before treatment of rats. Group I mice were treated with distill water 10ml/kg (negative control group). Group II mice were given 400mg/kg Diclofenac sodium (Positive control group). Group III were given 300 mg /kg of WE (Approximately 5 drops) by gastric gavage. Thirty minutes after treatment the reaction time was again evaluated at 0, 15, 30, 60, 90 and 120 minutes by dipping about 2-3cm of tail of each of the mice into a water bath containing warm water maintained at a temperature of 50±1°C . The time taken for the mice to flick its tail or withdraw it from water known as the pain reaction time (PRT) was recorded for all the mice.

Hot Plate Method: Fasted eighteen albino mice of either sexes were casually divided into three groups (n=6) of six mice in each group. All were fasted for 12 hours but provided clean drinking water. Before treatment, its reaction time was determined at 0, 15, 30, 60, 120 and 180 minutes intervals, The mean of these six determinations constituted the "initial reaction time " ie. Reaction time before treatment of rats. Group I mice were treated with distil water 10ml/kg (negative control group). Group II mice were given 4000mg/kg Diclofenac sodium (Positive control group). Group III were given 300 mg of WE (Approximately 5 drops) by gastric gavage. Thirty minutes after treatment the reaction time was again evaluated at 15, 30, 60, 90 and 120, minutes. Each of the mice was placed on a hot plate maintained at the temperature of 55±1°C and the pain reaction time (PRT) or latency period determined with a stop watch was recorded which indicates the time taken for the mice to response to the pain stimulus. The response to pain stimulus considered including jumping, rising, and licking of hind foot.

Data Analysis

Statistical Analysis: The data were represented as the mean ± standard deviation. SD. Results were analysed by one-way ANOVA variance followed by multiple comparison of tukey's t-test. *P < 0.05 values are considered as statistically significant when compared to control.

RESULTS

Acute Toxicity Test: Acute toxicity test of the Electrohomeopathic medicine WE produced no death or signs of toxicity after 24 hours even at the dose of 3000mg/kg which shows that the WE was well tolerated. They did not develop any adverse symptom even after two weeks.

Acetic Acid Induced Writhing Reflex: The effect of WE on the acetic acid-induced abdominal constriction in mice is presented in Table -1. The result shows that the WE , and the reference drug Diclofenac sodium significantly increase pain threshold and reduced abdominal writhing($p < 0.05$) in mice when compared to the negative control group. Also the WE caused increase in percentage protection from 0% negative control group to 52% test groups. (Table -3)

Tail Immersion Method: The outcome of tail immersion test in mice is put forwarded in Table -2.

Table 2. Phytochemical constituents of Electrohomeopathy medicines WE

Sl. no	Phytochemical constituents	Name of test	Result
1.	Alkaloid	1. Mayer's reagent 2. Hager's reagent 3. Wagner's reagent 4. Dragendorff's reagent	++ ++ ++ ++
2.	Glycosides	Borntrager's test Legal test	++ +
3.	Flavonoid	Shinoda's test: Lead acetate solution test	++ ++
4.	Phenols and tannins	Ferric chloride test:	++
5.	Amino acid	Millon's reagent test:	+
6.	Carbohydrates	Molish test	+
7.	Steroids	Liebermann–Burchard test	++
8.	Saponins	Foam test	++
9.	Terpenoids	Noller's test	++

Table 3. Analgesic activity of WE by Acetic Acid Induced Writhing Reflex

Group	Treatment	Mean number of Writhing	% protection
I	Distil water	8.2±7.94	0
II	Diclofenac sodium	4.2±7.46	48.29
III	White Electricity	4.1.0±4.29	52.73

Table 4. Effect of analgesic activity of Electrohomeopathy medicine WE by tail flick method.

Groups	Increase in Reaction time (second) in different time intervals.(minute)						
	Basal reading	**0 min**	**15 min**	**30 min**	**60 min**	**120 min**	**180 min**
Control	2.4±0.4	2.8±0.2	2.8±0.2	2.8±0.2	2.8±0.2	2.8±0.2	2.8±0.2
Standard	2.4±0.4	2.4±0.4	6±0.3162**	8.4±0.2449**	8.4±0.2449**	8.6±0.2449**	8.8±0.2449**
Test	3±0.5	3±0.1	4.8±0.3742*	5.4±0.2449**	8.4±0.2449**	9±0.3162**	9.2±0.2634**

Values are expressed in mean ± SD, (n=6), one-way ANOVA followed by Tukey's t-test. *Indicates $p<0.05$ level of significance and**Indicates $p<0.01$ level of significant difference.

Table 5. Effect of analgesic activity of Electrohomeopathy medicine WE by Hot-plate method.

Group	**Basal reading**		**0 min**		**15 min**		**30 min**		**60 min**		**120 min**		**180min**	
	PL	JR	PL	JR	PL	JR	PL	JR	PL	JR	PL	JR	PL	JR
Control	3.6 ±0.244	3.8 ±0.2	8.2 ±0.2	8.6 ±0.6782	3.4 ±0.2449	7 ±0.3162	5.8 ±0.5831	11.2 ±0.3742	7.2 ±0.2	10 ±0.3162	10.4 ±0.2449	12 ±0.3162	12.8 ±0.3164**	13.6 ±0.3168**
Standard	3.8 ±0.2	3.8 ±0.2	13 ±0.4472	13.2 ±0.3742	5.4 ±0.2449	7.8 ±0.3742	9.2 ±0.2**	9.6 ±0.2449*	10.2 ±0.2**	10.4 ±0.2449	11.6 ±0.2449*	12.6 ±0.2449	12.2 ±0.3246**	13.4 ±0.3468**
Test	3.6 ±0.118	3.6 ±0.2449	9.6 ±0.5099	10.4 ±0.9274	8 ±0.4472**	12.2 ±0.9695**	11.8 ±0.7348**	13 ±0.4472**	13.4 ±0.24498**	14.6 ±0.2449**	14.6 ±0.2449**	14.4 ±0.6**	15.4 ±0.4246**	15.8 ±0.2446**

Values are expressed in mean ± SD, (n=6), one-way ANOVA followed by Tukey's t-test. *Indicates $p<0.05$ level of significance and** Indicates $p<0.01$ level of significant difference.

The result exhibits that the WE and the standard drug Diclofenac sodium significantly increased the PRT when compared to the negative group. (Table - 4)

Hot Plate Method: The outcome of the effect of WE on the hot plate method is presented in Table -3. The result exhibits that there was no remarkable difference in the PRT during the pre drug testing time. After drug and WE administration, comparing the pre and post during PRT using T-test showed that the standard drug Diclofenac sodium and the Electrohomeopathic medicine WE significantly increased the PRT (Table -5)

DISCUSSION

Pain is an invalidate complement of many medical complaints and pain is one of the most salient restorative priorities (11) Analgesics are the drugs used to reduce pain and the classical analgesics drugs are principally opoid analgesics and nonsteroidal anti-inflammatory drugs. They may be the origin of natural products or many are synthetic compounds. On prolonged or repeated use of synthetic molecules, they may be associated with serious side effects such as ulceration, gastrointestinal bleeding, additive potential, respiratory distress, drowsiness, nausea etc. (12, 13). So, there is need for the exploration of bioactive compounds from natural products particularly from medicinal plants for use of alternative analgesics with little or no side effects.

In aboriginal system of medicines many plants and herbs have been used for the treatment of pain. Elecrohomeopathic medicine WE has been used by local Electohomeopathy practitioners for the treatment to releive different type of pains like headaches, short traumatic injury, arthritis, myalgia, neuropathic pain and even to relive pain from cancer and pain exerted due to radiotherapy too. The present study was therefore undertaken to investigate the analgesic activity of Elecrohomeopathic medicine WE with the aim of establishing the pharmacological basis for the local practitioner's use to treat for pains of different kinds. From the study it was remarked that the experimental model of analgesic activity the Elecrohomeopathic medicine WE displayed analgesic effect and has both peripheral and central analgesic properties. Its central analgesic activity was established through tail-flick and hot-plate method and its peripheral analgesic property was confirmed by a writhing test. Effect of the Elecrohomeopathic medicine WE on tail flick is primarily a spinal reflex and is examined to be selective for central acting analgesic compounds like opoid derivatives (morphin, pethidine), while peripheral analgesics is known to be inactive on this type of painful stimulus(14,15). Nociceptive pathways activated in the tail flick and hot plate tests are not the same. So in dissimilar anti-nociceptive tests the same opoid ligand can evoke different responses even through the same receptors involved (16, 17). The PRT of WE exhibited by tail flick method is quite inspired when compared to the 'Basal reading' of control and standard group (Table -2) and similarly the PRT of WE

exhibited by Hot plated method is also quiet encouraged when compared to the 'Basal reading' of control and standard group in form of paw leaking (PL). Jumping (J), and rising (J) (Table -3). The reduced abdominal writhing and increase in percentage protection from 0% negative control group to 52% was the evidence of peripheral analgesic activity was exhibited by WE (Table -3). Its peripheral analgesic activity was confirmed from its inhibitor action on acetic induced nociptive stimuli. The intraperetonial injection of acetic acid increased the mediators of pain mainly prostaglandin E2 and prostaglandin 2α which evoked writhing (18, 19). Moreover acetic acid also increases the vascular cell permeability, mast cell degranulation, and smooth cell contraction. Eosinophils and chemotaxis stimulate the nociceptor and produce pain response. Peripheral analgesic effect of WE may be mediated by prostaglandin inhibition, whereas the central analgesic action of WE probably mediated through inhibition of central pain receptors. Analgesic effect of WE exhibited after 15 minutes of its administration and lasted even at 3hours This expresses that chemical constituents of WE showed pharmacological action has rapid onset of action and of the short duration of action. Though WE is formulated from blending of the spagyric essence of 16 herbs, literature study reveals that each herb possesses tremendous anti-inflammatory and analgesic action.

One of the important *herb Achillea millefolium's* anti-inflammatory action is already proved (20, 21). Anthemis nobilis, another important herb of WE also possesses anti inflammatory effect which ultimately helps to ease pain (22). *Petrosalinum sativum* another herb also possesses antiniflammatory activity aids its contribution for pain relief. (23). Arnica monta a popular herb is quite famous to relief pain and its analgesic activity has been proved by several researchers. (24,25). *Guacum officnale*, a significant part of WE is well known herb is widely used by alternate medical practitioners to reduce pain (26). *Taraxcum officinale,* another important herb of WE also possesses anti-inflammatory effect which ultimately helps to ease pain (27). *Ruta graveolens's* pharmacology property reveals the analgesic action and as being a part of WE , it also aids synergism. *(28). Sanguisorba officinalis* also is a part of WE and possesses anti inflammatory activities. *(29). Sanguinaria Canadensis* also has potent anti-Inflammatory and analgesic activity and thus justifies action of WE. (30). Analgesic activity of *Taxus baccata* is evident for the analgesic action of WE. (31). *Avena sativa* monta a popular herb is quite famous to releive pain and its analges activity has been proved by several researchers.(32). Viscum album exerts anti-inflammatory effect by selectively inhibiting cytokine-induced expression of cyclooxygenase-2 as it is a part of WE , it mimics the analgesic action. (33). *Cimicifuga racemosa,* another important herb of WE also possesses anti-inflammatory effect which ultimately helps to ease pain. (34). *Menyanthes trifoalata ,* another important herb of WE also possesses anti inflammatory effect which ultimately helps to subside pain. (35).

CONCLUSION

The above results indicate that Electrohomeopathic medicine WE possesses significant analgesic activities. Therefore, this scientific study justifies the use of WE medicines for relieving of all kinds of pains by local Electrohomeopathic practitioners. Further research is essential to isolate the phytochemical constituent which is principally responsible for the analgesic action of WE.

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Conflict of interest

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