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Original Article

Disease Monitoring System- Microbiological Examination of Haloperidol -22 Ointment

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ABSTRACT

Haloperidol is a high-affinity sigma(1) receptors especially Guinea pig brain or rat liver membrane in tris-HCl buffer at pH:8.00. Our aim is to identify and investigate fungus infected skin infections inclusive of metabolic disease and HIV infection in Asian and African black race community, rehabilitation and chronic alcohol withdrawal side effects symptoms. Implementation of sustainability factor using 7R principle specially reduction sustainability in Haloperidol ointment-22 out of rethink, refuse, reuse, repair, repurpose and recycle disease monitoring in skin disease patients. Our microbiological test results degradation reaction is mapped with non-degradation reaction in synthetic qualitative test using FC-reagent. Our formulation was designed as a innovative ratio proportion method 1:13.33 active ingredient Haloperidol and papain-urea debridement ointment and developed microbiological examination using sequence addition of amla rust, softrot and anthracnose fungus incorporation with ointment formulation. These formulations were framed using factors such as impaired immunity, loss of hair, ammonia accumulation, impair vision, and clot retraction. Deep learning model algorithms is proposed to diagnose disease detection, optimum classification - reaction, classification - probability, classification-skin application time using original data set 418 softrot, 214 blue mould, 513 rust, 490 healthy. Out of three amla fungus disease blue mould investigations as utilized for treatment of skin disease drug addiction patients especially rehabilitation procedures. Finally concluded that haloperidol-22 ointment was shown in the zone of inhibition on the 66th day of microbiological test. Degradation reaction was stopped at 81st day.

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Introduction

Psoriasis

Immune-mediated disease that is characterized by inflammation caused by dysfunction of immune system which in turn inflammation in body psoriasis in combination with psoriatic arthritis and different co-

morbidity conditions such as cardiometabolic, hepatic and psychological comorbidity requires interleukin (IL)-17 and interleukin (IL)-23 inhibitor, turnover necrosis factor-biologic inhibitor, dimethyl furanate inhibitor. Complex interferences inclusive of T-cells, dendritic cells, keratinocytes with IL-23/Th-17 axis being chronic inflammation and keratinolytic proliferation could be inhibited by incorporation of papain and urea-ointment base [1].

Haloperidol

Behavioral issues [2-3] related to psychotic problems are linked with mesolimbic pathway blocking post synaptic D2-Dopamine receptors. Presence of butyrophenone, fluorophenyl group, P-chloro phenyl group, piperidine ring are responsible for anti-psychotic activity, potency with lipid solubility, affinity with CNS penetration, receptor interaction, three carbon responsible for spatial arrangement which could result blocking dopamine receptor. Haloperidol is one of the earliest agents approved for the suppression of motor and vocal tics in Tourette syndrome. Its D2 receptor antagonism reduces the hyperkinetic movements and vocalizations associated with basal ganglia dopaminergic dysregulation [4-5].

Papain

Papain acts as a debris-removing agent, with no harmful effect on sound tissues because of the enzyme's specificity, acting only on the tissues, which lack the $\alpha 1$ antitrypsin plasmatic antiprotease that inhibits proteolysis in healthy tissues. The mechanism of biochemical removal of caries involves cleavage of polypeptide chains and/or hydrolysis of collagen cross linkages.

Papain enzymes have a long history of being used to treat sports injuries, other causes of trauma and allergies. It has previously been reported that minor injuries heal faster with papain proteases than with placebos. Papain also has been successfully used to overcome the allergies associated with leaky gut syndrome, hypochlorhydria (insufficient stomach acid) and intestinal symbiosis like gluten intolerance. Papain has previously been reported to have significant analgesic and anti-inflammatory activity against symptoms of acute allergic sinusitis like headache and toothache without side effects [6-7].

Urea

Maintaining Healthy Skin Products with low or medium concentration (2%– 20%) of urea may be indicated for routine skin care in individuals without skin disorders.

The skin of patients with AD is characterized by increased TEWL and dysfunction of the skin barrier.

The use of emollient and moisturizing creams is considered a cornerstone of the management of this disorder. Urea-containing preparations have been shown to decrease TEWL and improve hydration of the stratum corneum and water-binding capacity in eczematous skin. The use of topical urea at concentrations ranging from 4% to 20% has been documented in multiple clinical trials.

Xerosis in patients with diabetes mellitus: Xerosis is frequently observed in diabetic patients and can increase the risk of skin infection and ulceration. In RCT of 40 individuals with type 2 diabetes mellitus, a 5% urea-based formulation with other ingredients such as arginine and carnosine increased skin hydration and significantly decreased xerosis compared to a glycerol-based emollient.

Urea -based formulations can improve hydration of the stratum corneum and its water retention capacity and decrease TEWL, pruritus, desquamation and hyperkeratosis inpatients with psoriasis. High urea concentration (40%–50%) can be an excellent alternative in the treatment of localized hyperkeratotic plaques of psoriasis. Urea at 40% together with bifonazole 1% can be effective in the management of scalp psoriasis. Keratolytic action in vitro and in vivo studies have established the emollient and keratolytic properties of urea. Common study endpoints include reduction of TEWL, stratum corneum hydration, and clinical assessment. Urea has been shown to change certain physical properties of the skin. Early studies have shown that urea can induce conformational changes in proteins by causing unfolding, solubilization, and denaturation.

By possibly breaking hydrogen bonds and interfering with the quaternary structure of keratin, urea disperses and denatures keratin without disrupting the epidermal water barrier. Several studies have also shown that urea decreases the DNA synthesis index of epidermal cells, leading to a thinning of the epidermis and reduction of basal epidermal cells. An early hypothesis was formed that pretreatment or concomitant treatment with urea can enhance efficacy of other topical therapies. Salicylic acid is frequently combined with urea to produce a significant keratolytic effect. Urea can enhance debridement in vascular and diabetic ulcers [8].

Haloperidol ointment-22 is helpful in treatment of rehabilitation, skin allergic symptoms, drug induced histamine release allergy, alcohol and drug withdrawal symptoms and OUD disease conditions [9-11].

Methodology

Chemical Structure

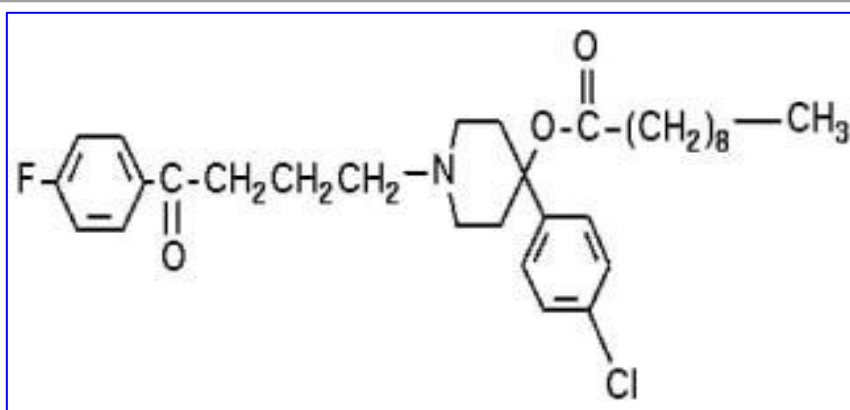


Figure 1: Structure of Haloperidol.

Modification of procedural importance via structural analysis

The butyrophenone moiety was the focus of the first modifications, and these Modifications are referenced to haloperidol. Reduction of the carbonyl to methylene group 5 (D2 Ki = 24.0 nm) resulted in a 27-fold decrease in binding to the D2 receptor compared to haloperidol. Replacement of the carbonyl group with Sulphur 6 (D2 Ki = 8.8 nm) and oxygen 7 (D2 Ki = 5.3 nm) resulted in more moderate decreases in affinity at the D2 receptor. Overall, with the piperidinol in place, the carbonyl appears to be an important group for binding to D2 receptors but is not a necessary group since it can be replaced by a methylene group, Sulphur, or oxygen to display potent binding at the D2 receptor. The trend in binding at the D2 receptor is an increase from the methylene group to sulphur and then to oxygen. Binding to the D3 receptor for the three compounds shows little or no observable pattern although the sulphur analogue displayed the highest potency among them. At the D4 receptor, the sulphur analogue displayed over 24-fold decrease in binding while the oxygen analogue displayed over 4-fold increase in binding compared to the methylene analogue. A significant observation relates to the binding of two of the compounds to 5HT receptor subtypes. Compound 7, the oxygen analogue, displayed a 49-fold increase in binding (Ki = 74.0 nm) at the 5HT1A receptor while compound 6 bound with a moderate increase in affinity (Ki = 317.0 nm) compared to haloperidol. At the 5HT2A receptor, the methylene substituent had a moderate binding affinity while the sulphur (Ki = 72.0 nm) and oxygen (Ki = 93.0 nm) analogues displayed increased binding over haloperidol. The next SAR focus was on the piperidine moiety. Removal of the alcohol function from compounds 6 and 7 to form 8 and 9 respectively resulted in significant decreases in binding to the D2 receptor. the piperazine analogue of haloperidol produced a substantial decrease in affinity to the D2 receptor from

0.89 nm to 253.5 nm. Removal of 4'-fluoro atom while retaining the 4-chloro atom 17 did not result in an increase in binding but instead led to significant decreases except for the 5HT1A receptor where binding increased by a factor of 3 (5HT1A, Ki = 19.8 nm) [12-14].

Formula

Step:1: Sample Preparation Procedure (Trituration Method)

- All apparatus were cleaned using cotton soaked in ethanol and allowed to dry.
- Eight Haloperidol tablets were selected from the sampling package (22I-22 XIII).
- The tablets were placed in a mortar and triturated using a pestle to obtain a fine powder.
- Four grams of papain-urea ointment base was accurately weighed using a weighing balance.
- A small quantity of the ointment base was transferred onto the ointment slab.
- A small portion of the powdered Haloperidol was added to the ointment base on the slab and mixed thoroughly using an ointment spatula.
- The mixing was performed within a 10 × 10 cm area to ensure uniform incorporation and spreading motion.
- The remaining powder and ointment base were incorporated gradually with continuous mixing until a smooth and homogeneous ointment was obtained.
- 15 minutes mixing of Ingredients and 20 minutes slide drag mixing to evaluate Spreadability characteristic. The empty Petri dish (lid and base) was weighed using a weighing balance before transferring the prepared ointment
- The prepared ointment was transferred into the weighed Petri dish, properly labelled for identification, and stored for 24 hours for further qualitative tests [15-24].

- k. The same procedure was repeated to prepare four additional batches of the ointment.

Step 2: Microbial Test

Haloperidol ointment-22 was prepared with the composition of papain 4000 mg, urea 2.6 g, haloperidol 1200 mg, and excipients 788 mg, making a total weight of 5990.69 mg (≈ 5.99069 g). This means that approximately 6 g of ointment contains 1.2 g of haloperidol as the active ingredient. This formula was mapped with social responsibility key social content and rehabilitation procedure [25-27]. Parallel plate method was tested using the microbial evaluation was using microscopic slides as In-Vaso-constrictive activity-7 mins the Vaso constrictive activity-Haloperidol ointment-22 was dropped down using Lithium carbonate-4 mins.

Take sample (1 loop) with addition of microbes. White turn into green colour. First 24hrs, Green colour was observed. After this, a three-fold quantity of ointment was added to the sample. A colour change or modification were occurred at 24 hours. On the 21st day of observation, a gel-like consistency was noted. At the end of the 56th day, colour changed with a Gel-like consistency was observed. At end of 61st day, the gel-like consistency, same colour, was observed. At end of 66th day same gel like consistency was observed.

At the end of the 67th day, colour deterioration was started up. Chemical reaction has stopped up at the end of the 81st day.

External application procedure at chemical deterioration 81st day

$$81 \times 24 = 1944 \text{ hrs}$$

External application before chemical deterioration 66th day

$$66 \times 24 = 1584 \text{ hrs}$$

$$1944 - 1584 = 360 \text{ hrs}$$

360 hrs difference in chemical reactivity (start – end up)

$$360 \text{ hrs} \div 24 \text{ hrs} = 15 \text{ days}$$

Time of application (Successful rate) = 15 days

Step 3: Biological Investigation Method

Comparative assessment micro-biological test versus qualitative test procedure

Chemical reactivity I was compared and tested using Folin–Ciocalteu reagent. Yellow colour was observed using fructose and albumin. The moiety in reaction of amino acid interaction with ninhydrin using calcium as catalyst. Binding efficiency was achieved with the formation of yellow colour. In addition, Folin–Ciocalteu reagent was used in qualitative synthetic chemical evaluation. (Subra Scientific Company,

Pondicherry). But chemical reactivity happened at the 66th day turn off mixing black anon white into white colour.

Chemical Reactivity – II was compared and tested using the Folin–Ciocalteu reagent. A greenish purple to green colour was observed using albumin without and the addition of fructose in the reaction of amino acid interaction with ninhydrin using calcium as a catalyst. Binding efficiency was achieved after the addition of the Folin–Ciocalteu reagent with the formation of a green colour. Same chemical reactivity happened on the 24 hours-first end day, 1-21st end day microbiological test examination after incorporation one-fold addition of microbes equivalent to 200 mg amla blue mould.

Chemical Reactivity – III: Chemical reactivity was observed and tested using the Folin–Ciocalteu reagent with 3ml alcohol addition. A blackish colour was observed using albumin with the addition of fructose in the reaction of amino acid interaction with ninhydrin using calcium as a catalyst. Binding efficiency was achieved after the addition of the Folin–Ciocalteu reagent with the formation of a black colour. Same chemical reactivity happened on the 45 th day after incorporation threefold addition of microbes equivalent to 600 mg amla blue mould.

Chemical Reactivity – IV: Chemical reactivity was observed and tested using the Folin–Ciocalteu reagent with excess 7 mL alcohol. Fading of purple colour was observed using fructose, ninhydrin, albumin, and CaCO_3 . Different chemical reactivity happened on the 56th day after incorporation threefold addition of microbe's equivalent to 600 mg amla blue mould at 21st day test sample. Black sand white coloration, Gel like consistency were shown in microbiological test instead of fading of purple colour in chemical test.

Chemical reactivity – V was observed and tested using Folin–Ciocalteu reagent in excess addition (7 mL). A bluish ash colour was observed using fructose, albumin, calcium carbonate, and Ninhydrin reagent. Black and white colouration, Gel like consistency and quantity reduction happened in ointment formulation during microbiological test instead of bluish purple colour in chemical test using total of 17 mL.

Chemical reactivity – VI was observed and tested using Folin–Ciocalteu reagent in Haloperidol ointment-22 in combination with lithium carbonate. A fading of violet colour was observed. Finally, excess alcohol and the lithium carbonate combination with Haloperidol ointment 22 resulted in the fading of the violet colour, which prevents deterioration reactions. But chemical reactivity happened especially sustainability reduction happened at the 66th day due to sequence addition 200

mg,600 mg and 600 mg of amla blue mould via promoting degradation reaction which turn off mixing black and white into white colour.

Step 4: Disease Monitoring System-Identification of zone of inhibition

7-fold addition of amla blue mould and alcohol

Chemical equation:

Amla (Rust) + Haloperidol-22 ointment $\longleftrightarrow$

Furfural in amla blue mould produces addition compounds.

Degradation started up due to drug loss

Zone of inhibition was identified at 66th day



Figure 2: 56th Day Examination



Figure 2: 66th Day Examination

At the end of the microbiological test results, Haloperidol Ointment-22 was useful in the treatment of post-operative skin, side effects after (4-5 days) cancer treatment, Radiation treatment, skin side effects (14-15 days application time), Opioid intake skin side effects (2.5 days application time), metabolic disease-related skin side effects (after approximately 8 days of application time) [28-30].

Step 4: Confirmation degradation- reaction mechanism

Loss on Drying

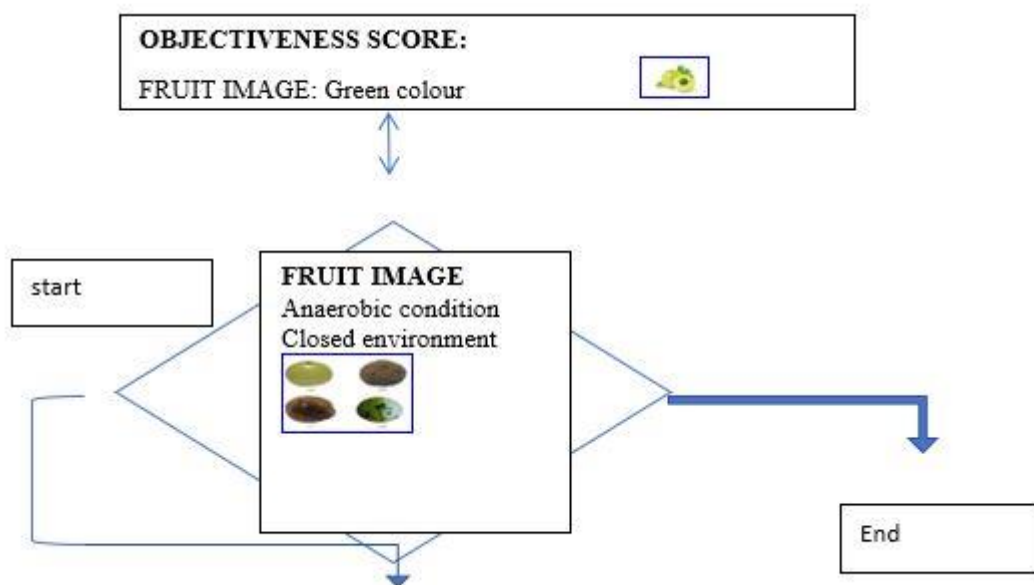
Weighed 1.5 g Haloperidol-22 ointment and dried in oven at 100°C or 105°C for 3 minutes under two consecutive weightings do not differ by more than 0.5 mg of each gram of substance, Cooled in desiccator. loss on drying sample:1: 34.61% spreadability index:15.18 minutes, Loss on drying sample:2:30.61%, spreadability index:17.63minutes [31-32]. Stability were shown at 145°C, 160°C. Degradation was started up at 200°C. chemical reactivity -degradation reaction happened at the 67th day due to addition of 1400 mg microbes and 15 mL of alcohol with coupling effect of 1200 mg haloperidol -22 ointment. Above 200°C

temperature, Ointment physical state was reversed into reduced solid mass. Stoppage of chemical degradation occurred at 81st day sample.

Results and Discussion

Manual detection of phyllanthus emblica disease could result in an error in identifying disease. CNN and YOLO-V2 based on Deep learning is proposed to detect fungus Anthranose: Phomopsis Phyllanthi as a variety of anthracnose, Collectotrichum gloeosporioides as a variety of soft rot and ravenelia emblicae as a rust fungus variety. Sustainability factor was implemented on disease infected amla fungus that can reduce quantity of haloperidol-ointment 22 within 66 days. Microbes in furfurals diffuse across cell membrane and induces intracellular accumulation of reactive oxygen species (ROS) leading to redox imbalance and potential damage to cellular structures like mitochondria. Restructuring skin surface using keratinolytic substance like urea. Repairing implementation -urea cycle can modify and balance redox potential in mitochondrian region using carbomoyl phosphate synthase-1.

Disease Monitoring System



Deep learning model:

CNN Layer: Amla rust, softrot, anthranose

Data set: Class probability-(Fresh/late, colour, texture)

Tracing option: Disease monitoring system-Skin disease drug rehabilitation procedure

Microbial sample preparation



Classification output:

Soft rot: *Collectotrichum gloeosporioides*,

Anthranose: Phomopsis Phyllanthi

Rust: *Ravenelia emblicae*



Classification-Procedural instructions output

Five sets were prepared and evaluated.



Class -reaction probability[33-39]

Skin application timing

S.No	Week	Colour Identification
1.	I week	White turns Green colour
2.	II week	Low Green
3.	III week	Colour discolouration 3-fold addition microbes Gel like consistency
4.	IV week	Stable, Gel like consistency
5.	V week	Stable, Gel like consistency
6.	VI week	Stable, Gel like consistency
7.	VII week	Stable, Gel like consistency
8.	VIII week 3 rd day	Stable, Gel like consistency Colour deterioratio at 67 th day



Class-Comparison probability		
S. no	Internal Probability dosing	External Probability dosing
1.	192 hours 7 days	1584 hours 15 days
2.	Rehabilitation Drug addiction and Chronic alcohol withdrawal symptoms	Rehabilitation Skin infections Drug addiction and Chronic alcohol withdrawal symptoms



Class -chemical deterioration		
S. No	After Deterioration Stoppage Day	Before Deterioration Drug Loss Confirmation
1.	81 ST DAY-1944 HOURS No chemical reaction after 67 th day	66 TH DAY-1584 HOURS Zone of inhibition was identified



Class -Findings and conclusion		
S. No	Disease Conditions	Skin Application Timings
1.	Post-operative skin, side effects	4-5 days
2.	cancer skin treatment	14-15 days
3.	Radiation skin treatment	14-15 days
4.	Opioid intake skin side effects	2.5 days
5.	metabolic disease–related skin side effects	8 days
6.	Chronic alcoholic withdrawal Skin side effects	2.5 days
7.	STD and HIV -Antipruritics	Minimum timings:14-15 days

Conclusion

Deep learning -convulated algorithm implemented in classification output-microbiological test results on Haloperidol ointment-22. Blue mould amla was having 214 data set and augmented data set 540 as per conference stated in international conference on advances in computing communication and applied informatics. Sequence addition of 7-fold blue mould having augmented disease data set showing 1498 convulated disease layer-CNN into haloperidol ointment -22 and investigated 5.9 turns multiplied feature extraction data set 64x64x128 total of 256 in one round up microbial addition in execution 1498 feature extraction layer were reacted with haloperidol-22 ointment-1200 g which turns into white colour attained reduction sustainability factor. Zone of inhibition was observed on the 66th day of evaluation and stoppage of degradation reaction happened on the 81st day of microbiological test. So 1:13.33 ratio proportion haloperidol-22 ointment was proposed and skin disease specially recapitalization -drug addiction skin disease in a controlled sugar environment.

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Author's Contribution

Sengamalam Ravindran: Data curation, data analysis, drafting, writing, and formatting. Conceptualization, draft correction and editing, and suggestions for improvements.

Conflict of Interest

The authors declared no conflict of interest and no funding was required to conduct these review data.

Availability of Data and Materials

The data supporting this study findings will be made available upon request.

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