TARGETING CELL MEMBRANE POTENTIAL IN CANCER WITH TTX-HERBAL THERAPY

Assoc. Prof., Dr. Le Quang Huan, Dr. Ha Thi Thanh Huong
Hoa Binh University
Corresponding Author: htthuong@daihochoabinh.edu.vn

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Abstract

Objective: *The objective of this study was to develop and evaluate a natural formulation that modulates cell membrane potential as an adjuvant therapy for cancer. The formulation combines a low dose of Tetrodotoxin (TTX) with traditional Vietnamese herbal extracts to inhibit tumor growth, enhance immune responses, and improve patient quality of life.*

Methods: *The formulation, composed of pufferfish extract and traditional herbs (e.g., Codonopsis pilosula, Astragalus membranaceus), was tested in vitro on cancer cell lines, in vivo in animal models, and in a preliminary clinical trial. Key metrics included tumor size, immune markers, and patient well-being.*

Results: *The formulation effectively inhibited cancer cell proliferation by modulating membrane potential via VGSC (voltage-gated sodium channel) blockade. It significantly enhanced immune responses by stimulating the production of Interferon-gamma (IFN-γ). In a trial involving 27 liver cancer patients, average tumor size decreased by 35.4% after three months. Additionally, the formulation provided significant pain relief for patients with gastrointestinal and esophageal cancers. All participants reported improvements in overall health. The formulation was safe, with no significant adverse effects observed in animal studies or in patients who had undergone chemotherapy or radiotherapy.*

Conclusion: *The combination of low-dose TTX and herbal extracts shows promising potential as an adjuvant in cancer therapy. It not only suppresses tumor growth and enhances immunity but also significantly improves patients' quality of life. Further clinical studies with larger sample sizes are needed to confirm these findings.*

Keyword*: Pufferfish, Tetrodotoxin, Herbals, Cancer, Membrane Potential.*

Hướng đích điện thế màng tế bào trong điều trị ung thư bằng liệu pháp TTX-thảo dược

PGS. TS. Lê Quang Huấn, TS. Hà Thị Thanh Hương
Trường Đại học Hòa Bình
Tác giả liên hệ: htthuong@daihochoabinh.edu.vn

Tóm tắt

Mục tiêu: *Nghiên cứu này nhằm phát triển và đánh giá một công thức tự nhiên có khả năng điều biến điện thế màng tế bào để hỗ trợ điều trị ung thư. Công thức kết hợp liều thấp Tetrodotoxin (TTX) với các cao chiết thảo dược truyền thống của Việt Nam, nhằm ức chế sự phát triển của khối u, tăng cường đáp ứng miễn dịch và cải thiện chất lượng sống của bệnh nhân.*

Phương pháp: *Công thức được bào chế từ chiết xuất cá nóc và các dược liệu (như Đảng sâm Codonopsis pilosula, Hoàng kỳ Astragalus membranaceus, v.v.), được thử nghiệm in vitro trên các dòng tế bào ung thư, in vivo trên mô hình động vật, và trong một thử nghiệm lâm sàng sơ bộ. Các chỉ số chính bao gồm kích thước khối u, dấu ấn miễn dịch và mức độ cải thiện sức khỏe bệnh nhân.*

Kết quả: *Công thức cho thấy hiệu quả trong việc ức chế sự tăng sinh của tế bào ung thư thông qua điều biến điện thế màng bằng cách phong tỏa kênh Na^+ phụ thuộc điện thế (VGSC). Công thức cũng làm tăng đáp ứng miễn dịch bằng cách kích thích sản xuất Interferon-gamma (IFN-γ). Trong thử nghiệm trên 27 bệnh nhân ung thư gan, kích thước khối u trung bình giảm 35,4% sau ba tháng. Ngoài ra, công thức giúp giảm đau đáng kể cho bệnh nhân ung thư đường tiêu hóa và ung thư thực quản. Tất cả người tham gia đều báo cáo cải thiện sức khỏe tổng thể. Công thức an toàn, không ghi nhận tác dụng phụ nghiêm trọng trong mô hình động vật và ở bệnh nhân sau hóa trị hoặc xạ trị.*

Kết luận: *Sự kết hợp giữa TTX liều thấp và các cao chiết thảo dược cho thấy tiềm năng đầy hứa hẹn như một liệu pháp hỗ trợ trong điều trị ung thư. Công thức không chỉ ức chế sự phát triển của khối u và tăng cường miễn dịch mà còn cải thiện đáng kể chất lượng sống của bệnh nhân. Cần thêm các nghiên cứu lâm sàng với cỡ mẫu lớn hơn để xác nhận kết quả này.*

Từ khoá: *Cá nóc, tetrodotoxin, thảo dược, ung thư, điện thế màng tế bào.*

1. Introduce

The membrane potential is the electrical potential difference across the plasma membrane of a cell, playing a crucial role in maintaining normal cellular functions. Maintained at a resting membrane potential (RMP) of approximately -60 to -90 mV in healthy cells, primarily through the action of the ATPase pump and ion channels, acts as a "biological battery" that controls cell volume, cell cycle, differentiation, and signal transduction, ensuring cellular stability [1, 2].

Firstly, regarding changes in membrane potential in cancer cells: A significant hallmark of cancer cells is the shift from a deep hyperpolarized state in healthy cells to a depolarized state, resulting in a less negative membrane potential. This change is driven by the dysfunction of ion channels and pumps, leading to an intracellular ion imbalance [3]. In cancer cells, depolarization is not merely a symptom; it contributes to pathogenesis through various mechanisms including *Promoting Proliferation***,** a depolarized generates a "persistent proliferative signal," accelerating the cell cycle; *Increasing Metastasis***,** altered affects signaling, enhancing the migratory and invasive capabilities of cancer cells; and *Maintaining Cancer Stem Cells (CSCs)*, the depolarized state helps to keep CSCs in an undifferentiated state, making them difficult to eliminate.

Secondly, the hypothesis of cancer treatment by modulating membrane potential: Given the clear differences in membrane potential, researchers hypothesize that restoring the hyperpolarized state in cancer cells could serve as a novel therapeutic strategy. This hypothesis is supported by the following arguments including *Inhibiting Proliferation*, Restoring polarization can block the cell cycle at the G1 phase, preventing cancer cells from dividing; *Reducing Metastasis,* regulating can decrease the invasive and migratory abilities of cancer cells; *Promoting Differentiation and Apoptosis,* forcing cancer stem cells to differentiate makes them more sensitive to therapy, or directly inducing programmed cell death (apoptosis).

Thirdly, compounds that Support Cancer Treatment via Membrane Ootential: Numerous drugs and natural compounds are being investigated for their ability to modulate membrane potential by regulating ion channels or pumps to inhibit cancer progression. Notable examples including *Tetrodotoxin (TTX)*, a neurotoxin from pufferfish; and *TTX blocks voltage-gated sodium channels (VGSCs)*, inhibiting metastasis in cancer cells [7]; *Betulinic Acid (BA),* a compound from birch bark, BA modulates voltage-gated calcium channels (VGCCs) and mitochondrial ion channels, causing apoptosis in drug-resistant cancer cells; *Cannabidiol (CBD),* from cannabis or hemp, CBD acts through ion channels like TRPV2, altering membrane potential and suppressing proliferative signals in cancer cells; *Margatoxin (MgTX)*, a peptide from scorpion venom, MgTX selectively inhibits the potassium channel, causing intracellular accumulation and activating apoptosis, which is particularly effective against cancer stem cells.

In this study, we created a formulation containing a low-dose extract from pufferfish, which has tetrodotoxin (TTX). This compound specifically targets and modulates voltage-gated sodium channels (VGSCs) to restore the membrane's polarized state. The formulation was combined with extracts from various medicinal herbs: *Codonopsis Pilosula* to enhance immunity; *Astragalus Membranaceus* for its antioxidant and immune-boosting properties; *Rehmannia Glutinosa* to support cell regeneration; *Angelica Sinensis* to improve circulation and reduce inflammation; *Polygala Tenuifolia* for its neuroprotective and antioxidant effects; *Ligusticum Striatum* to enhance blood circulation and provide anti-inflammatory benefits.

2. Materials and Methods

Materials: The materials include pufferfish extract and various medicinal herbs: Codonopsis Pilosula, Astragalus Membranaceus (Fisch), Rehmannia Glutinosa (Gaertn), Angelica Sinensis (Oliv) Deils), Polygala Tenuifolia (Radix Polygalae), and Ligusticum Striatum (Ligusticum wallichii Franch).

Methods: The study utilized a range of biological, biochemical, and pharmaceutical assays to evaluate the product's effects on cell cultures, experimental animals, and human volunteers.

Formulation Development Composition of Herbal Extract Blend: Codonopsis pilosula (20%), Astragalus

membranaceus (20%), Angelica sinensis (10%), Rehmannia glutinosa (10%), Ligusticum chuanxiong (10%), Salvia miltiorrhiza (8%), Hedyotis diffusa (12%), Phyllanthus urinaria (10%), Pufferfish Liver Extract.

Formulation Preparation Method:

Herbal Extraction: Herbal powders are soaked in ethanol for 48 hours, filtered, and concentrated at 90-100°C to obtain a high-potency extract with moisture content <7%, rich in bioactive compounds.

Pufferfish Liver Extract (TTX) Preparation: Pufferfish liver is pulverized in an acetic acid solution (1:5 w/v, pH 2.0-2.5) and stirred overnight. The mixture is heated at 90-100°C for 10-15 minutes, centrifuged to remove proteins and debris, and concentrated to obtain a TTX-rich extract. TTX content is quantified via HPLC or bioassayed using Swiss albino mice (20-22 g). Per international standards, 1 Mouse Unit (MU) ≈ 0.22 µg TTX. The TTX dosage in the formulation is 30 ± 2 µg/day, administered in two divided doses.

Blending: Herbal extracts are combined in specified ratios with TTX in a controlled environment to ensure uniformity and stability.

Packaging: Formulated into capsules and stored in a dry, light-protected environment.

Determine the Toxicity of the Preparation

Acute and subchronic toxicity studies were conducted at the Military Medical Academy, following the guidelines of Abraham WB (1978), Turner A (1965), the Vietnamese Ministry of Health (1996), and the World Health Organization (WHO) for drug toxicity research.

The subchronic toxicity of the formulation was specifically evaluated in rabbits, following Abraham's method and WHO/Ministry of Health regulations for the efficacy and safety of traditional medicines. Rabbits were divided into three groups of 10: (1) Control group: Received 0.9% sodium chloride solution at a dose of 2 ml/kg/24h for 42 consecutive days; (2) Test group 1: Received the formulation at a dose of 1,000 mg/kg/24h for 42 consecutive days; (3) Test group 2: Received the formulation at a dose of 1,500 mg/kg/24h for 42 consecutive days.

Evaluation Criteria: *Physiological-Pharmacological*: General condition, activity levels, food intake, body weight, and electrocardiogram (ECG) were monitored; *Hematological*: Red blood cells, hemoglobin, white blood cells, and platelet counts were measured; *Biochemical*: Levels of AST, ALT, urea, and creatinine were analyzed; *Histopathological*: On day 42, the rabbits were euthanized, and gross anatomical observations of the liver, spleen, and kidneys were performed. Tissues were then biopsied for histopathological examination. Blood for biochemical and hematological analysis and ECG readings were taken at three time points: baseline (T0), after three weeks (T3), and after six weeks (T6).

Follow-up Duration: Six weeks. The product's efficacy was tested on volunteer patients with liver and gastric cancer at the Military Hospital 108.

3. Results and Discussion

3.1. Results of the Acute Toxicity Study of the Formulation

White mice were divided into groups. Each group of mice was administered the formulation orally at gradually increasing doses. The condition of the mice and the survival/mortality rate in each group were monitored for 72 hours after drug administration (Table 1).

Table 1. Acute Oral Toxicity of the Formulation

No.	Dose Used (mg/kg BW)	n	Number of Animals Died (after 72h)	Number of Animals Survived (after 72h)
Group 1	4,500	12	0	12
Group 2	6,000	12	0	12
Group 3	7,500	12	0	12
Group 4	9,000	12	0	12
Group 5	10,500	12	0	12
Group 6	12,000	12	0	12
Group 7	13,500	12	0	12
Group 8	15,000	12	0	12

After administering the preparation at the highest dose of 15,000 mg/kg body weight, which is the maximum dose that can be orally administered to mice, no experimental mice died after 72 hours of observation. Since it was not possible to increase the oral administration volume further (the maximum drug volume that can be introduced into the stomach of white mice within 24 hours), the LD_{50} of the preparation in white mice via oral administration could not be determined.

Determine Subchronic Toxicity

Based on the analysis of the provided biochemical and hematological indices, here is the biopharmaceutical assessment:

Body Weight (BW)

BW increased significantly across the time points (T0, T3, T6) in all three groups (control, formulation dose 1, formulation dose 2). This indicates a statistically significant change in BW over time, which could be due to the natural growth process or an effect of the formulation.

However, there was no significant difference between the groups (). This suggests that the formulation at both doses did not cause a different effect on body weight compared to the control group.

Heart Rate, QRS Amplitude, Red Blood Cells (RBC), Hemoglobin (Hb), White Blood Cells (WBC), Platelets, AST, ALT, Creatinine, and Urea

All these parameters showed no statistically significant difference between the groups at time points T0, T3, and T6. This indicates that the formulation at both doses did not cause significant changes compared to the control group for the surveyed biochemical and hematological indices.

Similarly, there was no significant difference between the time points within each group, with the exception of body weight. This suggests that these indices remained stable over time and were not affected by the formulation.

The formulation at both doses (Dose 1 and Dose 2) did not cause a significant impact on the biochemical (AST, ALT, creatinine, urea) and hematological (RBC, Hb, WBC, platelets) indices compared to the control group, demonstrating the biological safety level of the formulation during the 6-month study period.

The increase in body weight was the only statistically significant change, but this is likely related to the natural development process rather than the effect of the formulation, given the lack of difference between the groups.

The stability of parameters such as heart rate, QRS amplitude, and other biochemical indices suggests that the formulation did not cause clear adverse effects on cardiovascular, liver, kidney function, or the hematopoietic system.

The tested formulation exhibits a good level of biological safety, causing no significant changes in the biochemical and hematological indices, apart from the increase in body weight over time (likely due to natural factors). Further research is needed to evaluate long-term effects or other aspects of the formulation (Table 2).

Table 2. Biochemical and Hematological Analysis Results

Indicator	Time Point	Control Lot (Mean ± SD)	Group used dose 1 (Mean ± SD)	Group used dose 1 (Mean ± SD)	P (between lots)
Body Weight (kg)	T0	1.94 ± 0.11	1.94 ± 0.08	1.95 ± 0.10	> 0.05
	T3	2.27 ± 0.10	2.25 ± 0.08	2.26 ± 0.06	> 0.05
	T6	2.40 ± 0.09	2.37 ± 0.08	2.41 ± 0.10	> 0.05
p (between time points)		p_{3-0}, p_{6-3}, p_{6-0} < 0.05			
Heart Rate (beats/min)	T0	245.40 ± 35.37	258.80 ± 42.29	263.20 ± 28.16	> 0.05
	T3	256.20 ± 37.36	251.00 ± 30.93	250.80 ± 28.96	> 0.05
	T6	248.20 ± 29.42	259.00 ± 43.70	253.00 ± 29.86	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
QRS Amplitude (mV)	T0	0.375 ± 0.052	0.399 ± 0.082	0.356 ± 0.119	> 0.05
	T3	0.392 ± 0.095	0.379 ± 0.057	0.381 ± 0.092	> 0.05
	T6	0.371 ± 0.050	0.391 ± 0.086	0.375 ± 0.074	> 0.05

p (between time points)		> 0.05	> 0.05	> 0.05	
Red Blood Cells (10^{12}/L)	T0	5.46 ± 0.96	5.35 ± 0.50	5.98 ± 0.94	> 0.05
	T3	6.25 ± 1.22	5.75 ± 1.29	6.53 ± 1.40	> 0.05
	T6	5.72 ± 0.43	5.53 ± 0.38	5.73 ± 0.80	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
Hemoglobin (g/L)	T0	114.50 ± 20.50	132.10 ± 18.42	124.50 ± 20.45	> 0.05
	T3	133.50 ± 21.33	122.80 ± 26.28	120.80 ± 18.28	> 0.05
	T6	123.00 ± 10.55	134.30 ± 25.71	136.10 ± 19.73	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
White Blood Cells (10^9/L)	T0	5.28 ± 1.11	4.79 ± 0.95	5.00 ± 1.32	> 0.05
	T3	4.82 ± 1.10	5.16 ± 1.26	4.73 ± 1.15	> 0.05
	T6	4.59 ± 1.08	4.95 ± 1.24	5.11 ± 1.24	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
Platelets (10^9/L)	T0	259.40 ± 52.35	295.40 ± 75.38	290.00 ± 63.86	> 0.05
	T3	267.50 ± 34.01	291.00 ± 60.36	265.70 ± 42.69	> 0.05
	T6	274.90 ± 27.04	297.90 ± 47.61	287.50 ± 52.56	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
AST (IU/L)	T0	60.45 ± 18.08	55.83 ± 19.38	53.46 ± 20.74	> 0.05
	T3	55.08 ± 18.12	58.24 ± 19.42	68.10 ± 15.16	> 0.05
	T6	56.93 ± 18.11	64.20 ± 21.36	57.67 ± 17.85	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
ALT (IU/L)	T0	53.80 ± 22.54	56.83 ± 20.92	52.30 ± 21.12	> 0.05
	T3	62.40 ± 19.84	56.10 ± 18.98	58.60 ± 19.43	> 0.05
	T6	58.16 ± 19.28	60.37 ± 17.53	54.48 ± 20.67	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
Creatinine (µmol/L)	T0	67.56 ± 12.55	60.70 ± 15.93	54.30 ± 17.71	> 0.05
	T3	57.40 ± 15.56	56.80 ± 14.89	63.80 ± 14.97	> 0.05
	T6	55.40 ± 17.30	59.80 ± 15.99	59.60 ± 17.79	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	
Urea (mmol/L)	T0	3.65 ± 1.30	3.99 ± 0.98	3.29 ± 1.00	> 0.05
	T3	3.85 ± 1.30	3.46 ± 1.11	4.06 ± 1.09	> 0.05
	T6	4.01 ± 1.37	3.68 ± 0.98	3.55 ± 1.18	> 0.05
p (between time points)		> 0.05	> 0.05	> 0.05	

Notes:

- White Blood Cells (10^9/L) means the number of white blood cells measured in units of 10^9 cells per liter of blood.

- T0: before the experiment, T3: month 3, T6: month 6.

- $p > 0.05$: no statistically significant difference.

- Only body weight changed significantly between time points ($p < 0.05$).

- *Study Groups (Control*, Group used dose 1, Group used dose 2)

- *Group used dose 1 (use 1,000 mg/kg/24h, continuously for 42 days). Group used The dose 2 (a dose of 1,500 mg/kg/24h, continuously for 42 days).*

Analysis of Clinical Trial Results

This small-scale clinical trial demonstrates promising outcomes after a three-month treatment period. The results suggest (Table 3) the treatment has a positive effect on tumor reduction, liver function, and the general health of the patients.

Tumor and Biomarker Reduction: There was a significant 34.5% decrease in average tumor size. This is a strong indication that the treatment has an effective anti-tumor activity. This finding is further supported by the 50.12% reduction in AFP (Alpha-fetoprotein) concentration, a key tumor marker for liver cancer. A sharp drop in AFP levels typically correlates with a positive response to treatment.

Improvement in Liver Function: The data shows a marked improvement in liver health. The liver enzymes SGOT (AST) and SGPT (ALT), which are elevated during liver damage, decreased substantially by 53.11% and 60.24%, respectively. Additionally, Bilirubin levels, which can indicate poor liver function when high, were reduced by 24.79%. These results collectively point to a significant restoration of liver function and a reduction in liver cell injury.

Enhanced General Health: A notable 9.28% increase in average body weight is a very positive sign. Weight loss is common in cancer patients, and this weight gain suggests an improvement in the patients' overall nutritional status and well-being.

In summary, the treatment appears to be effective in not only reducing tumor size and activity but also in significantly improving liver function and the overall physical condition of the patients. While these results are highly encouraging, the small scale of the trial means that a larger, more comprehensive study would be necessary to validate these findings.

Table 3. Comparing Clinical Indicators Before and After 3 Months of Treatment

Monitored Indicators	Before Treatment	After 03 Months of Treatment	Decrease (%)	Increase (%)
Average Tumor Size	6.7 ± 2.1 (cm)	4.39 ± 1.8 (cm)	34.5	-
AFP Concentration	332 ± 143 (ng/ml)	165.6 ± 23.8 (ng/ml)	50.12	-
SGOT (AST)	93.2 ± 13.5 (U/l)	43.7 ± 5.2 (U/l)	53.11	-
SGPT (ALT)	123 ± 21.7 (U/l)	48.9 ± 9.7 (U/l)	60.24	-
Bilirubin	23.8 ± 12.7 (mmol/l)	17.9 ± 5.3 (mmol/l)	24.79	-
Weight	47.4 ± 5.8 (kg)	51.8 ± 2.3 (kg)	-	9.28

Discussion

The formulation proposed in this study represents a strategic approach, combining traditional herbal extracts with a potent bioactive compound, tetrodotoxin (TTX), to achieve comprehensive therapeutic potential for cancer, particularly liver cancer. This combination not only leverages the distinct pharmacological properties of each component but also generates synergistic effects, enhancing treatment efficacy and minimizing adverse effects.

The central role of TTX lies in its ability to specifically inhibit voltage-gated sodium channels (VGSCs) on neuronal and muscle cell membranes [1, 2]. With strictly controlled dosing (30 ± 2 µg/day), TTX blocks the influx of Na^+ ions into cells, thereby inhibiting membrane depolarization and preventing the initiation and propagation of action potentials [3]. This mechanism provides potent pain relief, particularly effective in managing neuropathic pain and refractory pain commonly experienced by cancer patients, thus improving their quality of life [6]. Furthermore, recent studies indicate that certain sodium channels, including VGSCs, play a role in the proliferation, metastasis, and survival of cancer cells [4, 5]. Consequently, TTX may interfere with these signaling pathways, contributing to its potential anti-tumor effects, particularly in inhibiting the growth of breast cancer cells and other cancer types [4].

Herbal extracts play a crucial

supportive role, synergizing with TTX. Active compounds from *Hedyotis diffusa*, *Phyllanthus urinaria*, and *Salvia miltiorrhiza* provide hepatoprotective effects, supporting detoxification and liver function recovery, consistent with observed reductions in AST and ALT levels in clinical trials. Additionally, *Astragalus membranaceus*, *Codonopsis pilosula*, and *Angelica sinensis* enhance qi and blood, improve patients' general condition, and promote weight gain (an average increase of 9.28%), while also boosting the immune system to aid the body in combating disease. This combination is expected to produce a synergistic effect, with TTX delivering robust modulation of neural signaling and direct anti-tumor activity, while the herbal extracts provide comprehensive support, reducing side effects and promoting recovery.

Regarding safety, acute and subchronic toxicity studies have confirmed the high biosafety of the formulation. An oral LD_{50} exceeding 15,000 mg/kg indicates low acute toxicity, ensuring safety at therapeutic doses via oral administration. In subchronic toxicity assessments, the stability of hematological parameters (red blood cells - RBC, hemoglobin - Hb, white blood cells - WBC, platelets) and biochemical markers (AST, ALT, creatinine, urea) after six weeks of high-dose administration (multiple times the therapeutic dose) demonstrates that the formulation does not harm the hematopoietic system, liver, kidney, or cardiovascular function. Rigorous quality control, including precise quantification and monitoring of TTX content through HPLC or bioassays in mice, is a critical factor in ensuring the safety and consistency of the preparation.

Despite the promising preliminary results, including reductions in tumor size, AFP levels, improved liver function, and weight gain in patients, certain limitations must be acknowledged. The small scale of the clinical trials, lacking randomized and double-blind control groups, necessitates larger phase II/III trials to confirm long-term efficacy and safety. Furthermore, the detailed molecular mechanisms of the formulation, particularly the interactions between TTX and herbal extracts in anti-cancer effects and the role of TTX in cancer-related sodium channels at therapeutic doses, require further investigation [5, 6]. Future research should focus on evaluating chronic toxicity (e.g., over 6 months or 1 year) and the pharmacokinetics (absorption, distribution, metabolism, excretion) of low-dose TTX in humans to optimize treatment regimens and ensure maximum safety.

Conclusion

The proposed formulation, integrating traditional herbal extracts with tetrodotoxin (TTX), demonstrates promising therapeutic potential for cancer treatment, particularly in alleviating neuropathic pain and inhibiting tumor progression while supporting overall patient recovery. The synergistic effects of TTX's targeted sodium channel inhibition and the hepatoprotective and immunomodulatory properties of herbal components highlight a novel approach to comprehensive cancer care. Preliminary clinical outcomes, including reduced tumor size, improved liver function, and enhanced patient well-being, underscore its efficacy. However, larger-scale, randomized controlled trials and detailed mechanistic studies are essential to validate long-term safety and optimize therapeutic protocols. This formulation represents a significant step toward integrating traditional and modern pharmacological strategies for improved cancer management./.

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