Hydrogel-Based Drug Delivery Nanoparticles with Conventional Treatment Approaches for Cancer Tumors; A comparative study using MCDM Technique

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Abstract

Cancer is a disease caused by the uncontrolled division of abnormal cells in a part of the body leading to cell damage or death (Apoptosis). This could result in the death of the host carrier. Most death cases of cancer patients have been linked to the systematic administration of therapeutic agents (chemotherapy) and other conventional methods as the preferred treatment approach for cancer therapy. This treatment mortality is associated with side effects, off-target accumulation, toxicity, and rapid renal and hepatic clearance. In recent times, scientists have researched on targeting tumor sites and enhanced retention of constant drug delivery to tumors to mitigate side effects, and toxicity-related challenges. Water-containing polymers called Hydrogels is a unique discovery by scientist and researchers for highly effective drug delivery systems for cancer therapy. Drugs loaded into these hydrogels remain relatively stable owing to the network-like structure and organic tissue-like consistency of these drug delivery systems. This study is focused on comparing hydrogel-based drug delivery systems with other conventional methods of cancer therapy using the Multicriteria decision-making (MCDM) method called fuzzy Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE). The comparison is based on certain criteria and assigned weights of importance. The results from this study indicate that hydrogel-based therapy with a net flow of 0.1457 is the most favorable and optimum therapeutic approach for the general treatment of cancer diseases. Followed by surgery with a net flow of 0.1415, and hydron therapy, immunotherapy, and radiation therapy came third, fourth, and fifth with net flows of 0.0489, -0.0858, and -0.1062, respectively. Chemotherapy with a net flow of -0.1441 was the least ranked alternative. This study demonstrates that the approach taken will be beneficial and supportive in providing answers for healthcare decision-makers who are dealing with uncertainty issues and that it can be enhanced with the availability of more alternatives, and criteria, and by assigning weights of importance to the specific conditions of the individual cancer patients.

Keywords: Cancer, Hydrogel, drug delivery, PROMETHEE, decision-making

1. Background

Cancer is a serious mortality factor that is caused by the uncontrolled division of abnormal cells in a part of the body leading to cell damage or death (Apoptosis) which could result in the death of the host carrier [1]. Cancer is regarded as the world’s second deadliest disease which has caused major mortality in the world. Cancer accounted for 10 million death Worldwide in 2020 [2]. Comparing the death toll rate to the rapidly growing world population, the mortality rate has decreased pragmatically from the preceding death toll rate in previous years. Records of mortality rate in 2018 were 9.6 million and 7.6 million in 2007 [2]. Owing to the rapid growth of the world population every year and comparing it to the slow rate of mortality cases due to cancer, one could logically conclude that cancer death cases are increasing at a slow pace compared with the rapid population growth of the world. This is only due to the improved therapeutic methods employed by researchers and scientists in recent years [2].

Most mortality cases of cancer patients have been traced to the systematic administration of conventional therapeutic agents (chemotherapy, radiation, surgery, and immunotherapy) as the preferred treatment approach. [1], [2]. These conventional treatment approaches are known to be associated with side effects, off-target accumulation, toxicity, and rapid renal and hepatic clearance [3]. In the past decades, researchers have studied a system of drug delivery that has
the capacity of targeting tumor sites and enhancing the retention of therapeutic agents to tumor sites in order to mitigate side effects, and toxicity-related challenges [4].

Anti-cancer drug delivery systems have been improved to achieve greater targeting selectivity and better delivery efficiency[5]. Localized drug delivery has been considered the most reliable and efficient way to deliver therapeutics, [5], [6], but this also has been greatly challenged by poor biodegradability, high immunogenicity, poor drug retention efficacy, and inability to constantly sustain the release of antitumor agents at the affected site. Researchers and scientists have successfully, through the application of Hydrogels, circumvented the hurdles of non-efficient drug delivery systems and deficient localized drug administration systems [3]. Hydrogels have proven to be highly reliable and biocompatible materials that allow for the versatile design to afford smart sensing and therapy at the same time [7]. Smart hydrogels can respond to environmental stimuli (e.g. heat, pH, light, and ultrasound), enabling a controlled and sustained drug delivery environment, which greatly enhances the efficiency and easy release of anti-tumor agents [8]. Drugs loaded into this hydrogel-based drug delivery system remain relatively stable owing to the network-like structure and organic tissue-like consistency of these drug delivery systems [8]–[10].

Oncologist through the scientific development of more treatment options for cancer has dived into the promising and more efficient treatment method for tumor necrosis. Conventional methods have been greatly challenged with their accompanying side effects.

Arruebo et al., [2] in their review study on the assessment of the evolution of cancer therapies discussed extensively, the conventional methods (chemotherapy, surgery, radiation, immunotherapy), and promising recent therapeutic methods (gene therapy and nanomedicine). But, hydrogel as an efficient drug delivery system was not considered in the study.

Deb et al. in 2020 used the Markov decision process to access cancer treatment options [11]. Wang et al. [7] deployed machine learning methods, general regression, and Cox proportional hazards regression to predict the effectiveness of treatment in patients with breast cancer. Ozsahin et al. [1] evaluated cancer treatment alternatives using the fuzzy Preference Ranking Organization Method for Enrichment Evaluations (PROMETHEE) Method. The study compared conventional alternatives such as; chemotherapy, radiotherapy, surgery, immunotherapy, and hormone therapy. Hadron therapy was added as a recent therapeutic approach for cancer. All approaches were evaluated and compared based on the following criteria; treatment duration, cost of treatment, comfortability, side effects, and percentage of survival rate. The results from the study showed that hadron therapy has the highest survival rate, short treatment time, and noninvasiveness and tops the list of alternatives when ranked with the fuzzy PROMETHEE method. Hydrogel-based drug delivery systems have not been considered an alternative for treating cancer tumors.

This study is focused on comparing hydrogel-based drug delivery systems with other conventional methods of cancer therapy using one of the analytical multi-criteria decision-making (MCDM) techniques specifically fuzzy PROMETHEE. This study is an improvement on the previous study that used a similar methodology for comparing cancer treatment approaches. The inclusion of a hydrogel-based drug delivery system for comparing other conventional methods of cancer therapy, and the modification of criteria for evaluation, comparison, and ranking. The comparison is based on the following criteria; use in isolation, cost of treatment, side effects, survival rate, tumor necrotic rate, reliability, pain relief rate, recovery period, complications during use, retention rate, and treatment time. The treatment techniques evaluated in this study are explained in detail below.

2. Treatment Approaches for Cancer Disease

2.1. Hydrogel-Based Drug Delivery Systems

Hydrogels are a 3-dimensional, hydrophilic, cross-linked polymeric network that has the ability to swell or de-swell and still retain a significant fraction of water within their structure [9]. They will never dissolve in water, and they have the potential for development in drug delivery systems. The most important properties of hydrogels are that they swell in the presence of water and shrink in the absence of water. Hydrogels are intelligent systems because they can respond to environmental stimuli like temperature and pH changes thereby effect changes in their physical or chemical behavior, resulting in the release of entrapped drugs in a controlled and sustained manner [8]–[10].

Cancer therapy in the past decades relied completely on the use of several drugs derived from biological sources from different bacteria and viruses. among others, these bio-based drugs get easily degraded and therefore inactivated on administration into the body without getting to the affected region [5]. Thus, the need for effective drug delivery to, and release of these drugs at target sites is of great importance. Drugs released from Hydrogels can be controlled and
sustained at the target site by designing them to swell and de-swell in response to certain stimuli, or slight changes in conditions, like temperature or pH changes. The customization of hydrogels could be done from synthetic polymer poly (ethylene glycol) diglycidyl ether and the sulfur-containing organic compound cystamine. And this makes them respond to prevailing temperature and pH by swelling and shrinking. It has been noted that the pH of the tumor microenvironment fluctuates between 5.5 and 6.5 owing to glycolysis in the tumor cells [5][10].

There are two kinds of hydrogels, they include synthetic and natural. Natural and synthetic polymers are known to be effective drug delivery polymers to target tissues [12]–[14]. To reach the targeted tumor tissue, polymeric nanoparticles stay in the bloodstream for a sustainable amount of time without being eliminated. They must exhibit nontoxicity, biocompatibility, and biodegradability [15]. Natural polymers such as starch, chitosan, alginate, hyaluronic acid, silk, gelatin, collagen, fibrin, and glycosaminoglycans attracted researchers’ interest because of their unique advantages like abundance, nontoxicity, biocompatibility, and biodegradability [15]–[17]. Cellulose is one of the abundant natural polysaccharides usually used as a hydrogel because of its excellent biocompatibility, and biodegradability [18].

Chitosan is another natural polysaccharide, it is derived from chitin. Chitosan shows improved solubility in water when used as a carrier. It has the ability to hold therapeutic agents at the tumor site due to its mucoadhesive cationic nature, thus facilitating a controlled drug delivery process. It is highly known for its controllable non-immunogenicity, controllable biodegradability, and availability [19], [20].

Dextran is another important polysaccharide usually converted into enzymatically biodegradable reaction and it is pH sensitive [18]. Xyloglucan and Collagen structures can also be used in the local delivery of therapeutic agents due to their flowability, injectability, biocompatibility, and network-like structural nature [21].

Gelatin is a highly biodegradable and biocompatible biopolymer protein that occurs in nature with a thermo-reversible property [22]. The gelatin in an aqueous solution solidifies at a temperature below 25 °C due to the formation of triple helices and rigid three-dimensional networks and it turns to liquid again when the temperature is raised to 30 °C due to the conformational changes from a helix to a more flexible coil [22]. Gelatin is therefore an effective drug delivery agent when combined with other polymers to show thermal gelation close to the body temperature [22].

Gellan gum is another polymer gotten from broth cultures of aerobic bacteria. The physical gelation ability of this polysaccharide makes it a suitable drug delivery agent. Physical gellan hydrogels are used for the preparation of tablets, beads, or microspheres. Interpenetrating polymer networks or co-cross-linked polymer networks made from gellan and other polysaccharides have also been developed as drug delivery systems [22].

2.2. Conventional cancer therapies

Conventional cancer therapies are existing known treatment approaches for cancer. They include chemotherapy, surgery, radiation therapy, immunotherapy, hydron therapy, etc. Table 1 gives a summary of the conventional cancer treatment approaches and their negative and positive aspects in the treatment of cancer disease.

2.2.1. Summary of The Cancer Treatment Options

a. Chemotherapy

Chemotherapy involves the use of anti-cancer drugs to initiate tumor necrosis [1]. These anti-cancer drugs could be administered orally or intravenously [3]. They make their way through the bloodstream to sites of cancer cells to initiate a high rate of tumor necrosis [1]. Chemotherapy is usually associated with off-targeting and this leads to the destruction of healthy cells in the surrounding that could cause different damages such as; hair loss, nausea, vomiting, fatigue, sores in the mouth, rashes on the hands/feet, diarrhea, dysfunction of the liver or kidney, etc. These side effects are traced to overmedication [23]–[28].

b. Radiation Therapy

This involves the use of an x-ray beam to kill cancer cells in the body [1], [23]. It works with the principle of electrical ionization, whereby charged particles in the body through the effect of radiation transfer energy from the rays to the cells of the body and thereby kill cancer cells or alter the genetic make-up of the cells to initiate cell necrosis. This process works with the mechanism of genetic alterations to damage the DNA so as to halt cell division which in turn causes necrosis of cancer cells [1], [23], [24]. In radiation therapy, the rays are able to kill cancer cells, and also,
ossification is produced in bone, and osteoclasts are diminished to cause tumor necrosis. Normal cells and healthy tissues are unnecessarily damaged. Damages could last for a lifetime for tissues or cells that cannot be regenerated. These side effects include stool leakage, fatigue, erectile dysfunction for males, vaginal irritation for females, fibrosis, scarring, neurological disorders, etc. Another challenge is off targeting the tumor site and the inability of radiation rays to reach some tumors site. E.g. chondrosarcomas in bone cancer are considered radioresistant tumors [1], [23], [24], [29]–[32].

c. Surgery

Surgery involves the manual removal of cancer tumors through the process of cutting through the skin with sterilized incision instruments after the administration of analgesic agents [1], [3]. A high local tumor control rate is achieved through surgery [29]. Surgery requires cuts through skin, muscles, and sometimes bone, these cuts can be painful and could lead to bleeding, infection, and even clotting of blood in some cases. Moreover, few cancer cells may remain around the affected site and could potentially result in cancer recurrence [1], [3], [23], [24], [29], [32]–[34].

d. Immunotherapy

This is the process of increasing or stimulating the immune system to fight against potential cancer cells or tumor cells in the body [4]. This can be achieved through the administration of immune-enhancing vaccines, monoclonal antibodies, therapeutic agents (drugs), cytokines, lymphocytes, or other biological immune modifiers used to increase or activate the immune system to promote an effective response against tumors [27]. This offers a long-lasting control for tumor cells without any chances of recurrence. It is often more targeted than other conventional methods of treating cancer cells. This can lead to an overstimulated or misdirected immune response which may cause a severe attack on other organs or fatal allergic reactions [4], [27], [35]–[40].

e. Hydron Therapy

This involves the use of a beam of (protons, neutrons, and other ions) to treat cancer (a precise form of radiotherapy) [1], [31]. Hydron therapy is a more tumor-targeting method used to control tumors in a more precise manner compared to radiotherapy. It has fewer side effects but is highly expensive and limited to some kinds of cancer [1], [31], [41]–[43].

f. Hydrogel-based therapy

This is a more advanced, safer, and accurate anticancer drug delivery system [3], [7], [13]. Unlike conventional methods of treating cancer, which target cancer cells as well as healthy ones, hydrogels allow you to give targeted doses to the affected sites only [7], [13], [14]. Hydrogels cannot cover large tumors especially if they are larger than 10 centimeters, therefore hydrogels can be used in conjunction with either chemotherapy, surgery, or radiation therapy [3], [7], [13], [14], [44]–[52].

3. Material and Methods

The evaluation, assessment, and comparison of the most preferred treatment approaches for cancer tumors have always been based on theoretical evaluations and precise experiments. Recently artificial intelligence methods have been deployed for the diagnosis and treatment of cancer and also for comparing diagnostic and therapeutic approaches to identify the most efficient approaches [53]. Many studies in literature have deployed different MCDM techniques to compare, rank, and evaluate different approaches for diagnosing and treating different cancer types. No existing study has compared hydrogel-based drug-delivery systems with conventional methods of treating cancer using the MCDM method called fuzzy-PROMETHEE. This study takes a unique approach to evaluate, rank, and compare different approaches for treating cancer disease including hydrogel-based drug delivery nanoparticles using the fuzzy PROMETHEE method. Only very limited studies have deployed this methodology for comparing diagnostic and therapeutic approaches for cancer tumors, therefore, this method is unique in its kind to this study.


MCDM techniques are part of the most widely used methods to identify the best decision in scenarios where multiple criteria are assigned with alternatives [54]. The MCDM methods are efficient methods with enormous benefits in the operational research field that involves the use of criteria to evaluate, rank, and compare a set of available alternatives [55]. MCDM is a method that brings together multiple criteria to produce a solution that requires agreement [56]. The
primary objective of MCDM is to assist decision-makers in deciding alternatives that correspond to their needs and is consistent with their preferred preferences. [56]–[59].

The analytic hierarchy process (AHP), a technique for order of preference by similarities to ideal solution (TOPSIS), elimination et Choix traduisant la réalité (ELECTRE), PROMETHEE, viseskriterijumska optimizacija I kaompromisno resenje (VIKOR), and data envelopment analysis (DEA) are some of the efficiently applied MCDM methods in different fields [53]. Each has its own set of advantages and disadvantages. Recent studies, however, have demonstrated the efficacy of PROMETHEE in a variety of medical applications [60], [61]. In order to make decisions based on multiple criteria, the PROMETHEE technique evaluates each alternative based on established criteria with pairwise comparison [62].

3.2. Fuzzy PROMETHEE

The PROMETHEE method is an MCDM tool that allows users to evaluate and rank options based on predefined criteria [63]. Brans and Vince developed the PROMETHEE method in 1985 [64]. With the PROMETHEE method, the user has complete control over the preference values of the criteria. PROMETHEE is widely used in a variety of fields. The weights assigned to the specified criteria and the preference function are the only necessary information from the decision-maker to determine how important the alternative is on each criterion. Because the PROMETHEE method still has difficulty dealing with vague data in real-world decision-making situations, fuzzy logic and the PROMETHEE are used in tandem [65].

Fuzzy logic can be thought of as a decision implementation design that integrates vague conditions into the decision process in its most basic form [65]. It can be used by decision-makers to evaluate non-crisp data also analyze systems using linguistic data while quantitative data is not available. The fuzzy logic theory was created and introduced by Zadeh in 1965 [66] to deal with the uncertainty of subjective judgment. Fuzzy set theory is used to formulate problems that are too complex to be solved by traditional methods of analysis. Various studies have combined fuzzy-PROMETHEE to compare, evaluate, and rank related alternatives to reach an appropriate decision based on criteria and assigned weights of importance to each chosen criterion [67]. Le Téno and Mareschal [68] were the ones who first proposed combining fuzzy set theory and the PROMETHEE method in 1998 [67], [69]–[76].

3.3. Application of Fuzzy PROMETHEE to the study

In this study, the fuzzy PROMETHEE method was deployed to evaluate the following proposed alternatives (chemotherapy, radiation therapy, hydrogel-based therapy, surgery, hydron therapy, and immunotherapy). The importance weights of criteria were assigned through an expert opinion. The criteria include; pain relief rate, side effects, survival rate, tumor necrotic rate, reliability, complications during use, recovery period, treatment time, cost of treatment, and use in isolation. Each of the considered criteria was defined using a linguistic fuzzy scale. Thereafter, the fuzzy data were defuzzified by the Yager index. Then, the PROMETHEE program was used for simulation using the Gaussian preference functions.

Selecting criteria importance levels for our comparison takes a critical procedure that requires expert opinions. The most important criteria are assigned a high weight, and the least important is assigned a lesser weight in fuzzy value as seen in Table 1. This process aids the decision-making process and creates a clear difference of relative significance between highlighted criteria.

<table>
<thead>
<tr>
<th>Table 1. Linguistic Fuzzy Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Linguistic scale for ranking</strong></td>
</tr>
<tr>
<td>Very High (VH)</td>
</tr>
<tr>
<td>High (H)</td>
</tr>
<tr>
<td>Medium (M)</td>
</tr>
<tr>
<td>Low (L)</td>
</tr>
<tr>
<td>Very Low (VL)</td>
</tr>
</tbody>
</table>

3.4. Parameters of The Analysis

The survival rate: Most treatment options carry some level of risk, which forces doctors to conduct extensive research on the safest course of action to be taken in order to give patients the best chance of survival. Patients are typically
encouraged to mentally prepare for the treatment approach they have chosen by being informed about the risks associated with using any of the available treatment modalities. Both patients and doctors look for the treatment option with the best survival rate.

**Pain relief rate:** Uncomfortable pains are frequently present with cancer disease. The highest rate of pain reduction is required by the decision-maker. All available treatment options lessen pain, but the option that provides the greatest pain relief is needed.

**Tumor necrotic rate:** Every used therapeutic strategy for cancer diseases has the potential to trigger tumor necrosis. Tumor necrosis is the death of tumors (tumor destruction). Maximum tumor necrosis is necessary for pain relief and to reduce the risk of tumor slow build-up recurrence. It results in the maximum elimination of tumors and prevents instances of potential recurrences of tumor buildup.

**Reliability:** This is the extent to which a particular treatment alternative can be trusted. Reliability is an important criterion for comparing treatment alternatives. A 0.92 weight of importance has been assigned to the reliability criterion to compare the study’s alternatives.

**The recovery period:** This is the expected time needed for the recovery of a treated patient following the administration of any treatment approach. The alternative that gives the fastest recovery to patients is considered favorable.

**Use in isolation:** The use of conventional cancer treatment modalities is often in collaboration. Chemotherapy is typically the first course of treatment, with surgery being the last resort if tumor metastasis (spread) and necrosis rates are both slow. As a result, treating cancer diseases has evolved into an expensive, time-consuming procedure with more side effects. A treatment strategy that can be used alone is preferable, less demanding, and has fewer side effects.

**Complications during treatment:** The available treatment approaches for cancer tumors are usually a complicated process. A treatment option that is quick to remove tumors, simple to use, and has a high targeting ratio is considered more advantageous for our comparison.

**Side effects:** Cancer disease treatments, particularly conventional methods, can have mild to severe side effects, depending on the treatment approach. Modern cancer tumor therapies, on the other hand, have greatly reduced any potential side effects.

**Cost of treatment:** The treatment option with the lowest cost is considered cost-effective and thus favorable to the patient.

**Treatment Time:** The time it takes to administer one complete treatment of cancer.

Table 2 shows the determination of parameters based on the aim, and important levels of criteria

<table>
<thead>
<tr>
<th>Criteria and Alternatives</th>
<th>Pain relief rate</th>
<th>Side effects (after effect)</th>
<th>Cost of treatment</th>
<th>Use in isolation</th>
<th>Survival rate</th>
<th>Tumor necrotic rate</th>
<th>Reliability</th>
<th>Recovery period</th>
<th>Complications during use</th>
<th>Treatment time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemotherapy</td>
<td>L</td>
<td>VH</td>
<td>H</td>
<td>NO</td>
<td>M</td>
<td>L</td>
<td>L</td>
<td>H</td>
<td>L</td>
<td>H</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>L</td>
<td>VH</td>
<td>H</td>
<td>NO</td>
<td>VH</td>
<td>M</td>
<td>M</td>
<td>H</td>
<td>VH</td>
<td>L</td>
</tr>
<tr>
<td>Surgery</td>
<td>VH</td>
<td>L</td>
<td>M</td>
<td>YES</td>
<td>VH</td>
<td>VH</td>
<td>VH</td>
<td>M</td>
<td>M</td>
<td>L</td>
</tr>
<tr>
<td>Hydrogel-based therapy</td>
<td>VH</td>
<td>L</td>
<td>H</td>
<td>YES</td>
<td>VH</td>
<td>VH</td>
<td>VH</td>
<td>L</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Hydron therapy</td>
<td>H</td>
<td>M</td>
<td>VH</td>
<td>YES</td>
<td>VH</td>
<td>VH</td>
<td>H</td>
<td>M</td>
<td>L</td>
<td>L</td>
</tr>
<tr>
<td>Immunotherapy</td>
<td>L</td>
<td>H</td>
<td>M</td>
<td>NO</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>H</td>
<td>L</td>
<td>H</td>
</tr>
</tbody>
</table>

### 4. Results/Discussion

The result after completing the ranking of alternatives using the fuzzy PROMETHEE method indicates that Hydrogel-based therapy with a net flow of 0.1457 is the most effective and ranked therapeutic approach for the general treatment of cancer diseases. Followed by surgery with a net flow of 0.1415, and hydron therapy, immunotherapy, and radiation therapy came third, fourth, and fifth with net flows of 0.0489, -0.0858, and -0.1062, respectively. Chemotherapy with a net flow of -0.1441 was the least ranked alternative, as shown in Table 3. However, the results may change if the weights of each criterion are altered.

Table 3: PROMETHEE flow table ranking alternatives
<table>
<thead>
<tr>
<th>Rank</th>
<th>Alternatives</th>
<th>Net Flow</th>
<th>Positive Outranking Flow</th>
<th>Negative Outranking Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hydrogel-based therapy</td>
<td>0.1457</td>
<td>0.1464</td>
<td>0.0008</td>
</tr>
<tr>
<td>2</td>
<td>Surgery</td>
<td>0.1415</td>
<td>0.1427</td>
<td>0.0011</td>
</tr>
<tr>
<td>3</td>
<td>Hydron therapy</td>
<td>0.0489</td>
<td>0.0729</td>
<td>0.0240</td>
</tr>
<tr>
<td>4</td>
<td>Immunotherapy</td>
<td>-0.0858</td>
<td>0.0172</td>
<td>0.1030</td>
</tr>
<tr>
<td>5</td>
<td>Radiation therapy</td>
<td>-0.1062</td>
<td>0.0205</td>
<td>0.1267</td>
</tr>
<tr>
<td>6</td>
<td>chemotherapy</td>
<td>-0.1441</td>
<td>0.0098</td>
<td>0.1539</td>
</tr>
</tbody>
</table>

When compared to previous studies that deployed fuzzy-PROMETHEE to rank alternative approaches for cancer treatment void of hydrogel-based therapy, it is clear that hydrogel-based drug delivery nanoparticles for the treatment of cancer have more efficacy compared to others. The result obtained from a study conducted by [1] showed that hydron therapy tops the list when compared with surgery, hormone therapy, immunotherapy, radiation therapy, and chemotherapy. Moreover, in contrast to the results achieved in that study, our study implemented a comparative evaluation with hydron therapy inclusive and found out that hydrogel-based drug delivery systems outperform hydron therapy with the following factors: highest pain relief rate, lesser side effects, better use in isolation, highest records of survival rate, more tumor necrotic functions, more reliable, shorter recovery time, less complicated, and more targeted tumor necrosis in shorter time.

A proper literature search is necessary to rank options appropriately and an expert opinion must be considered in any decision-making process.

Figure 1 shows a ranking of the options, highlighting their advantages and disadvantages. From most favored to least favored, each alternative is represented in this graph. The alternatives' advantages are shown by the values above the 0 threshold levels, while their disadvantages are shown by the parameters below the 0 thresholds.

![Figure 1: PROMETHEE Rainbow Evaluation Result](image)

5. **Conclusion**

The most effective methods of treating cancer diseases, which are the leading cause of mortality worldwide, are determined in this study using the F-PROMETHEE technique, which has been a successful decision-making tool. The findings of this study indicate that hydrogel-based drug delivery nanoparticles are the most favorable method of cancer therapy, followed by surgery, for the treatment of patient-specific cancer diseases. The least ranked option is chemotherapy. By identifying the effective course of treatment and its detailed features, this study helps both cancer patients and medical professionals.
This study also demonstrates that the analytical models can be integrated successfully in providing answers for healthcare decision-makers who are dealing with uncertainty issues and that it can be enhanced with the availability of more alternatives, and criteria, and by assigning weights of importance to criteria based on each patient's unique requirements dealing with cancer.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References


