Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Spl Issue [4] November 2022 : 239-246

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD

ORIGINAL ARTICLE **OPEN ACCESS**

In silico modeling for identification of radio protectors of Phyto- and Phyco-origin based on their bioactivity properties

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ABSTRACT

Ionizing radiation exposure has been reported to produce oxygen-derived free radicals in the tissue environment that have a tendency to donate oxygen to other substances. Free radicals induced oxidative damages to the biomolecules like lipid, protein and DNA is responsible for deleterious effects on living organism. Plants have been widely investigated for their potential activity against radiation damage in living organisms. Podophyllum hexandrum, Hippophaerhamnoides, Centellaasiastica, Tinosora cordifolia, Mentha piperata, Zingiber officinales, Spirulina plantensis, Chlorella vulgaris, etc., afford radiation protection. Screening of the large numbers of phyto/phyco ingredients can be done in a systematic and standardized approach by using in silico bio-prospection, which involves bioactivity parameter selection based on literature, priority indexing by random and advanced search model, scoring and decision matrix by using fuzzy set membership analysis, optimization and validation. This study will help to collect and analyze data systematically to obtain a logical output in terms of lead identification. Radio-protective activity of the resultant short-listedleads (agents/compounds of Phyto- and Phyco- origin) need to be further evaluated.

KEYWORDS: *Radio protective agents, natural products, protection, matrix modeling, ethno-pharmacology, in silico approach.*

Received 22.11.2022 Revised 13.12.2022 Accepted 21.12.2022

INTRODUCTION

Upon exposure of living organisms to ionizing radiation, oxidative stress may arise when free radical generations exceed their scavenging by bio regulatory defence mechanisms, resulting in some adverse alterations in biomacromolecules. Exogenous antioxidants may help in combating this oxidative stress. In cancer radiotherapy, non-cancerous tissues need to be safeguarded while malignant growths are being irradiated. A number of synthetic compounds, plant extracts and phytochemicals have been evaluated for their radio-protective activities. Synthetic antioxidants such as butylated hydroxyl-toluene and butylated hydroxyanisole failed on human patients because of the low therapeutic index and toxicity. Search for effective, nontoxic natural compounds with antioxidative activity is a grey area in radiobiological research [15, 1]. Nature has been a wellspring of restorative remedies for time immemorial. Natural products including a plethora of bioactive compounds from plants, have been used since ages, and emerged as source of novel chemotypes and pharmacophores in evidence-based drug discoveries [2]. The prospective of use of prospective products from novel microbial sources, especially those isolated from desiccated environment, is highly promising as potential drug leads in radioprotection [7]. With just 5 to 15 % of the roughly 250000 types of higher plants studied, and the capability of the marine climate scarcely tapped, these sections will stay a rich wellspring of novel bioactives [3]. Since only a very small fraction of the world's biodiversity has been explored for expected bioactivity, there is a large scope of systematically investigating these as promising radio-protectors. We have shortlisted selected natural products based on experiential learnings and the present knowledge of mechanisms of,cellular damage induced by ionizing radiation, for picking potential radio-protector leads. Our basic assumption is founded on the premise that ostensibly the phyto-chemicals scaffolds including exogenous antioxidants and other natural moieties possessing desirable pharmacological activities of relevance in radio-protection, can provide promising leads that need to be systematically explored and further optimized. The nutritional supplements and food ingredients has been the key focus for dealing with radiation induced maladies. In the present study, a combination of classical bio-prospection and *in*

silico approaches directed towards the discovery of potent radio protective agents from natural products has been presented. The classical bioprospection began with literature survey using ethno pharmacological literature while *in silico* part began with screening databases using random and relevant search model(s), scoring followed by decision matrix approach followed by validation. Current study resulted in discovering natural products through a systemic compilation and investigation of documented data to obtain a rational output for the identification of potential and promising radio protective phyto- and phyco- sources.

MATERIAL AND METHODS

a) Selection of natural products

Selection of natural products such as herbal plants and phyco ingredients were done according to their use in folk medicine and diversity in their chemical composition. As the study intended to find the potential natural products with radio protective for inclusion in foods, ingredients considered being safe for food use under the plants and sea weeds were selected.

b) Bioactivity parameters selection using classical approach

Bioactivity parameters were selected on the basis of study of literature of how radiation affects human body and factors which helps in the faster recovery. Radiation affects biological system either directly or indirectly and these effects can be controlled by these parameters and which are associated with natural sources. Ionizing radiation generates free radicals by radiolysis of water and this is the center point of all harmful effects caused by radiation. Out of all the eight parameter each one is having its own importance in radioprotection. Following are the eight parameters which are selected based on classical bioprospection approach Antioxidant activity, Haemopoietic stimulation, Metal chelation activity, Anti-inflammatory activity, Wound healing activity, Immunostimulant activity, Antiemetic activity and Antimicrobial activity. Rationale for the selection of each parameter is given in the Table I.

c) Assessment of relevance factor using 'keywords hits scoring matrix' approach

PubMed was used for Bioprospection studies. 'Best match' and 'Recent' were the two search models adopted for literature survey using the parameters. Search was done using keywords such as Bioactivity parameter + Radioprotection and yielded N hits. The first 20 hits were selected and they were categorized into relevant and irrelevant on the basis of observational analysis [12, 13]. This sample set based analysis evaluated 'net weightage linked to each bioactivity', using the formula:

Average Percentage Relevance =No of relevant hits based on observational analysis*N/n=20 x100

Relative weightage for each parameter assigned on the basis of percentage relevance were tabulated.

d) Selection of natural products using classical bio-prospection approach

Logical selection of natural products by classical bioprospection approach lead to in depth details about natural sources with respect to their radioprotective properties, dose reduction factor, food use, availability and ethnopharmacological importance. Rationale for the selection of plants based on the above mentioned factors is tabulated in Table I.

e) 'Binary coefficients matrix' to assess the presence/absence of a parameter in selected Herbals

Each of the selected plant is evaluated for the presence or absence of particular parameter. Evaluation is done by using Pubmed search engine. In which each plant along with bioactivity parameter is used as a key word for analysis ('Bioactivity Parameter + Selected Plant'). Plants which are having more than four parameters are screened for the next level analysis. Binary score (0-1) is given to plants which are having each property. It connects with the premise that plants acting in holistic way only ought to be evaluated for the subsequent examination.

f) 'Weightage matrix based analysis'

The overall weightage of the herbals were evaluated by multiplying their binary score with weightage obtained previously (plus equals one and minus equals zero). This approach is reported to remove the fake results which tend to usually happen due to investigator bias towards the selection of ingredients. This step enhances the 'vagueness factor' necessary for statistically important outcome [15]. Weightage matrix based analysis helps to identify the potential plant leads based on *in silico* bio-prospection. Identified plants were further assessed for advance analysis and optimization.

g) Fuzzy set membership analysis for decision matrix

Following mathematical relationship was used to calculate relevance of variety/products:

$\mu S = S\text{-}min(S)/[max(S)\text{-}min(S)]$ where μS represents the desirability values of members of the fuzzy set S, and Min(S) and max(S) are minimum and maximum values, respectively, in the fuzzy set S.

h) Optimisation of decision matrix score

Numerical values of scores obtained from fuzzy set membership analysis were converted in to leveled score by using a scaled magnitude representing star symbol.

RESULT

On the basis of the 'keyword hits scoring results', weightage to various parameters selected for screening of natural products comprising of phyto- and phyco- sources for radio protective properties, was decided according to the percentage relevance obtained for each parameter(Table 2). Highest percentage relevance was achieved for antioxidant activity, followed by other parameters like haemopoietic stimulation, metal chelation activity, anti-inflammatory activity, wound healing activity, immunostimulant activity, antiemetic activity and antimicrobial activity. As shown in Table2, the highest weightage of 4.29, was assigned to antioxidant activity. Out of the natural products examined, 10 plants and 02 phyco- ingredients were reported for five or more than seven characteristics pertaining to the mode of action of radiation protection. For example: *Curcuma longa* Linn., *Zingiber officinale, Spirulina platensis, Punica granatum, Moringa oleifera* Lam.,*Ocimum sanctum, Phyllanthus embelica, Centella asiatica, Aloe vera, Chlorella vulgaris, Acorus calamus* and *Tinosporacordifoila.*

The selected natural products were subjected to *in silico* bioprospection studies, wherein additive weightage matrix based analysis has been performed to analyze the weighted scores for each selected natural product on the basis of presence of each weighted parameter. This matrix works on dual principles of binary (0/1) and weightage scoring analysis combination.Two plants had a binary matrix score of more than or equal to seven(*Zingiber officinale* and *Curcuma longa* Linn.);Eight plants had binary matrix score equal to six (*Spirulina platensis, Punica granatum, Moringa oleifera Lam., Ocimum sanctum, Phyllanthus embelica, Centella asiatica, Aloe vera and Centella asiatica*) while twelve plants had the binary matrix score less than or equal to five (*Mentha piperita, Gingko biloba, Chlorella vulgaris, Aegle marmelos ,Acorus calamus, Myristica fragrance, Piper longum, Syzygiumcumini, Phyllanthus amarus or niruri, Mentha arvensis Linn., Biophytumsensitivum* and *Aphanamixispolystachya*).Of the ten plants and two phyco-ingredients selected on the basis of binary coefficient matrix, two plants namely*Curcuma longa* Linn. (score=21.01) and *Zingiber officinale* (scxore=19.18) showed immense potential of acting as a radioprotector against the harmful ionizing radiation with scores more than the median value score of 17.26 as shown in Table 4.*Curcuma longa* Linn. and *Zingiber officinale* were found to have the highest percentage relevance as shown in Table 5.*Curcuma longa* Linn., the common food spice known for its anti microbial and anti inflammatory properties held the topmost position with 100 percent relevance, followed by *Zingiber officinale*, another widely used spice with 70 percent relevance. Fuzzy set analysis of *Spirulina platensis, Punica granatum, Moringa oleifera* Lam.,*Ocimum sanctum, Phyllanthus embelica, Centella asiatica, and Aloe vera* indicated 39 percent relevance for radioprotection while *Chlorella vulgaris*had the least relevance percentage out of the 12 natural products selected by *in silico* bio-prospection approach. On the basis of optimized values *Curcuma longa* Linn. and *Zingiber officinale* were found to be the top two plants for radioprotection (Table.5).

Table 1.Rationale for selection of the bioactivity parameters for bio-prospection study

Sl. No.	Bioactivity parameter	Rationale for selection
1	Antioxidant activity	Ionizing radiation generates free radicals in a dose dependent manner and this radical reacts with our biomolecules and results in damages. Antioxidants can prevent oxidation chain reaction of free radicals by binding with them and thereby protects biological system.
2	Haemopoietic stimulation	Radiation can affect directly or indirectly. Directly it will cause damage to stem cells or progenitor cells and indirectly it can interfere with the communication pathways between the cells and the microenvironment. Compounds with hematopoiesis stimulating property at any levels stem cells, blood cells or progenitor cells etc. can mitigate aftereffects of radiation.
3	Metal chelation activity	Metals are vital components in the regular biochemistry of organisms.Compounds which can chelate metal ions renders radioprotection.
4	Anti-inflammatory activity	Radiation suppresses production of anti-inflammatory cytokines and induces certain signal transduction pathways. Compounds with anti-inflammatory property can stimulate production of cytokines and inhibit radiation induced signal transduction pathways.
5	Wound healing activity	Healing of radiation induced combined injuries (burns and wounds) will be delayed due to the suppressed immunity induced by radiation and complexity of wounds. Agents with wound healing activity can boost their recovery from combined injuries.
6	Immuno-stimulant activity	Spleen and cells of immune system are considered as the most radiosensitive parts of body .Radiation suppresses immunity power and thereby causes associated adverse effects in biological system .So many plant compounds are identified as that can stimulate immunity power and thereby contribute to radioprotection.
7	Antiemetic activity	Ionizing radiation exposure induces nausea , vomiting etc so that compounds which can prevent this symptoms will contributes to radioprotection
8	Antimicrobial activity	Antimicrobial activity is important to radioprotection because infection caused by translocation of intestinal gram negative bacteria is one of the main cause of death by radiation induced myelo-suppression. Antimicrobial compounds can prevent infections and provides protection.

Table 2. Weightage assigned to parameters based on Average Percentage Relevance

Sl. No.	Parameter chosen	Average Percentage Relevance (best match)	Average Percentage Relevance (Recent)	Mean value	RelativeWeightage assigned
1	Antioxidant activity	95.0	100.0	97.5	4.29
2	Haemopoietic stimulation	87.5	82.5	85.0	3.75
3	Metal chelation activity	92.5	77.77	85.135	3.75
4	Anti-inflammatory activity	80.0	77.5	78.75	3.48
5	Wound healing activity	53.25	55.75	54.5	2.41
6	Immunostimulant activity	30.0	75.0	52.5	2.33
7	Antiemetic activity	45.75	40.75	43.25	1.92
8	Antimicrobial activity	25.0	20.0	22.5	1.0

Table 3. Selection of natural products using classical bioprospection approach. (DRF is dose reduction factor; N.A. Not Available)

Sl No	Scientific name	Common name	Radio protective properties	DRF
1	*Acanthopanaxsenticosus*	Siberian ginseng, shigoka	Protects against radiation induced Suppression of hemopoiesis. Pre-irradiation administration of shigoka extract increased leukocyte counts and diminished cerebral haemorrhage .	N.A.
2	*Acoruscalamus*	Sweet flag	Protect prenatal irradiation induced development The comet parameters were found to decrease with postirradiation time, indicative of a decrease in radiation-induced DNA lesions due to DNA repair. The administration of the extract enhanced DNA repair, as can be inferred from the rate of postirradiation decrease of the comet parameters.	N.A.
3	*Adhatodavasica*	Malabar nut *adalodakam*	Leaf extract pre-treated irradiated animals exhibited radioprotection by an increase in GSH content and decrease in Lipid Per Oxidation (LPO) level. A significant increase in the serum alkaline phosphatase activity and decrease in acid phosphatase activity was also observed.	1.6
4	Aegle marmelos	Bael le	Administering mice with extract before irradiation reduced the symptoms of radiation sickness and delayed death..	1.15
5	*Ageratum conyzoides*	Goat weed	The treatment effectively protected mice against the gastrointestinal as well as bone marrow related death, as revealed by the increased number of survivors at all irradiation doses	1.3
6	*Allium cepa*	Onion	Provided protection against X-ray induced chromosomal aberrations	N .A.
7	*Aloe vera*	Aloe vera	Administering the mice with Aloe before ɣ- Irradiation delayed the onset and reduced the severity of radiation sickness. Aloe vera extract treatment pre and post irradiation resulted in protection against radiations by restoring the levels of Fe and Cu in the liver and intestine, intestinal Zn. Protected against oxidative stress	1.47
8	*Amaranthuspaniculatus*	Ragira Red shank	A. paniculatus leaf extract (600 mg/kg b.w./ day for 2 wks) protected mice against 5 Gy by reducing lipid peroxidation, glycogen and cholesterol levels in brain	1.36
9	*Aphanamixispolystachya*	AmooraRohituka, Pithraj tree	Extractprotects mouse bone marrow cells against radiation-induced chromosomal aberrations and this reduction in radiation-induced chromosome damage may be due to free radical scavenging and reduction in lipid peroxidation	N.A.
10	*Archangelicaofficinalis*	Mountain angelica	Administration of a combination ofrchangelicaofficinalis and Ledumpalustre extracts to mice 5–15 min before irradiation [7.5 Gy (LD 90/30)] rendered 70% survival	1.48
11	*Beta vulgaris*	Beet root	administration of beetroot extracts along with c-ray irradiation can induce significant decrease in the DNA damage and significant increase in proliferation and the stimulation of hematopoietic progenitor cells suggesting protective effects of beetroot against ionized irradiation	1.1
12	*Biophytumsensitivum*	Lajjalu mukkuthi	protective effect of *B. sensitivum*on Radiation-Induced haemopoietic damage is mediated through immunomodulation as well as sequential induction of IL-1beta, GM-CSF and IFN-gamma	N.A.
13	*Centellaasiatica*	Centella, gotu kola	Oral administration of the extract increased the survival time, reduced body weight loss in irradiated animals The extract significantly reduced the radiation induced	N.A.

			damage to DNA	
14	*Chlorella vulgaris*	chlorella	Oral administration of an algal mutant C. vulgaris E-25, 1 hr before or immediately after exposure to sublethal gamma-rays increased the number of endogenous spleen colony forming units (E-CFU). The magnitude of radioprotection was dependent on both, the dose of C. vulgaris fed and the time of administration	Pre treated 1.11 Post treated 1.15
15	*Coronopusdidymus*	Lesser swinecress	Free radical scavenging activity protected mice against radiations	1.07
16	*Curcuma longa*	Turmuric	Pretreatment with curcumin analog protects the hepatocytes against ɣ radiation induced cellular damage. Curcumin: copper(II) complex protected against irradiation by reducing the decline in levels of GSH, GST, SOD, Catalase and total thiols, and reduced lipid peroxidation .Curcumin prevents follicular Artesia in radiation induced apoptosis in ovarian follicles Curcumin pretreatment accelerated healing of irradiated wound	N.A.
17	*Glycyrrhiza glabra*	Licorice	70% methanolic extract protected rat microsomal membranes from ɣ radiation induced lipid peroxidation	N.A.
18	*Mentha arvensis*	Wild mint	Mint extract treatment protected the mice against gastrointestinal death and bone marrow related death	1.2
19	*Moringa oleifera*	Moringa	One hour prior i.p administration of 50% leaf methanolic extract showed significant radiation protection to bone marrow chromosomes in mice.	N.A.
20	*Myristica fragrance*	Nutmeg	Administration of MF significantly enhanced GSH and decreased testicular lipid peroxidationlevel whereas acid phosphatase and alkaline phosphatase activity did not show any significant alteration.. MF pretreatment effectively protected against radiation induced biochemical alteration as reflected by a decrease in LPO level and ACP activity, and an increase in GSH and ALP activity.	1.3
21	*Ocimum sanctum*	Holy basil	Flavonoids orientin and vicenin isolated from plant protected mice when either compound administered i.p. 30 minutes before irradiation, protected against the gastrointestinal syndrome and bone marrow syndrome.	1.37 (vicenin) 1.30 (orientin)
22	*Phyllanthusembelica emblicaofficinalis*	Amla	Ethanolic extract of amla(eAE) efficiently reduced pro-inflammatory cytokine (TNF-α and IL-1β) levels and appreciably upregulate anti-inflammatory cytokine (IL-10) concentration. Gastric ulcer healing induced by eAE was driven in a dose-specific manner through the harmonization of the antioxidative property and modulation of anti-inflammatory cytokine level.	1.12
23	*Piper longum*	Long Pepper	Ethanolic extracts of fruit reduced the elevated levels of Glutathione Pyruvate Transaminase, Alkaline phosphatase and lipid peroxidation in liver and serum of irradiated swiss mice	N.A.
24	*Podophyllumhexandrum*	Indian may apple	i.p administration of extract showed protection against the radiation induced damage in different types of cells 1present in testicular region. Partially purified fraction protected mice against lethal doses of ɣ irradiation Scavenged radiation inflicted free radicals and protected mice	N.A.
25	*Punicagranatum*	Pomegranate	Peel extract administering Protected mice against damage caused due to X- ray irradiation by reversing the leucocyte apoptosis and cell death reduction	N.A.
26	*Saracaasoca*	Ashoka tree	Hydro alcoholic extract showed radiation antagonistic property and reduced cytotoxicity and genotoxicity induced by irradiation of v79 cells with x rays .	1.39
27	*Spirulinaplatensis*	Spirullina	Extract caused a significant reduction of the micronucleus frequencies induced by gamma-radiation.. Results suggest that Spirulina modulate the radiation induced hematological and biochemical alterations in Swiss albino mice.	N.A.
28	*Tephrosiapurpurea .*	Wild indigo	Tephrosia extract (200 mg/kg b.wt) protected Swiss albino mice against radiation (5 Gy)-induced Haemopoietic injury. Showed selective effect on erythroid compartment by protecting against haemopoieticinjury.DRF 1.16	N.A.
29	*Zingiberofficinale*	Ginger	Hydro alcoholic extract exhibited radical scavenging capability and protected mice against radiation induced injury Reduces the severity of radiation sickness and mortality. Protects mice from GI and bone marrow syndromes.DRF 1.4	N.A.

Character weightage	Antiemetic activity	Immuno stimulant	Antioxidant activity	Metal chelation	Haemopoietic	Wound healing	Anti-inflammato	Antimicrobial activity	Score
Weightage	**1.92**	**2.33**	**4.29**	**3.75**	**3.75**	**2.41**	**3.48**	**1**	
Curcuma longa Linn.	0	1	1	1	1	1	1	1	21.01
Zingiber officinale	1	1	1	1	0	1	1	1	19.18
Spirulina platensis	0	1	1	1	0	1	1	1	17.26
Punica granatum	0	1	1	1	0	1	1	1	17.26
Moringa oleifera Lam.	0	1	1	1	0	1	1	1	17.26
Ocimum sanctum	0	1	1	1	0	1	1	1	17.26
Phyllanthus embelica	0	1	1	1	0	1	1	1	17.26
Centella asiatica	0	1	1	1	0	1	1	1	17.26
Aloe vera	0	1	1	1	0	1	1	1	17.26
Chlorella vulgaris	0	0	1	1	0	1	1	1	14.93
Acorus calamus	0	0	1	1	0	1	1	1	14.93
Tinosporacordifoila	0	1	1	1	0	0	1	1	14.85

Table4. Weightage Matrix Scores for herbal plants screened on basis of binary matrix scores

Sl No.	Plant	Score µs*	Optimized score
1.	*Curcuma longa* Linn.	1	********(8)
2.	*Zingiber officinale*	0.7029	*****(5)
3.	*Spirulina platensis*	0.3912	***(3)
4.	*Punica granatum*	0.3912	***(3)
5.	*Moringa oleifera* Lam.	0.3912	***(3)
6.	*Ocimum sanctum*	0.3912	***(3)
7.	*Phyllanthus embelica*	0.3912	***(3)
8.	*Centella asiatica*	0.3912	***(3)
9.	*Aloe vera*	0.3912	***(3)
10.	*Chlorella vulgaris*	0.0129	*(1)

Table 5. Fuzzy set membership analysis for natural products screened on the basis of weightage matrix scores

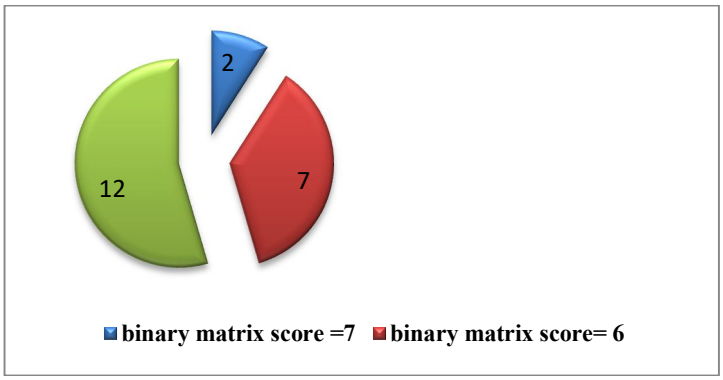

Figure 1.Selection of natural products using classical bio-prospection approach

DISCUSSION

Ionizing radiation can harm a molecule by ionization or reactions resulting in bond cleavage, or generation of free radicals that interact with the biomolecules, causing oxidative damage, incorrect

chromosomal segregation (misrepair) leading to mutation or cell death [2, 7, 10]. Radioprotectors mainly act by free radicals scavenging, enhancement of endogenous (enzymatic and non-enzymatic) antioxidants, and by stimulation of DNA repair, etc. [5]. Studies on development of radio-protectors were mainly carried out on synthetic compounds including glycosides, vitamins, and phosphorothioates (e.g.,amifostine).

Various natural products also possess antioxidants, apoptotic modulating, and growth regulating properties that show promising impact in repairing the ionizing radiation induced insults caused to cellular organelles. Many natural products like *Podophyllum hexandrum, Hippophaerhamnoides, Centellaasiastica, Tinosora cordifolia, Mentha piperata,Zingiber officinales, Spirulina plantensis, Chlorella vulgaris,* etc., have been studied for their radio protective efficiency. Bioactive constituents of various plant products also hold promise for radioprotection [1, 4, 9]. We have studied the classical literature based analysis along with*in silico* bio-prospection. This bio-prospection model was initially developed for targeting antibiotic resistance in human pathogenic microorganisms using herbal molecules [6].The eight parameters selected such as antioxidant activity, haemopoietic stimulation, metal chelation activity, anti-inflammatory activity, wound healing activity, immune-stimulant activity, antiemetic activity and antimicrobial activity, were on the basis of their direct significance in radioprotection. A multi-parametric approaches have been carried out on the natural products for potential radio-protective properties by assigning weightage to these parameters based on Average Percentage Relevance. (Table 2).Classical bio-prospection studies lays emphasis on ethno-pharmacological prominence, pragmatic uses, easy availability, and/or documented evidence-based indications (Table 3). Twenty-nine natural products showing variable significances with respect to parameters or descriptors chosen were shortlisted by the above investigatory methods. The analysis revealed that ten plants and two phyco- sources could be used for *in silico* cross matrix bio-prospection using binary coefficient matrix analysis to select the natural products of choice with highest significance out of all or none following the published procedure [9]. This analysis aided in removing the outliers and assisted in reduction of the database size to a measurable proportion [11]. The selection of plants followed the binary score of more than five and further scaled down to reduce the number of natural products need be systematically studied for radio-protective property (Fig. 1).The net scoring and the priority ranking with respect to the parameters useful in mitigation of radiation related injury and damage with respect to the overall radio-protective ability of the selected natural product (Table 4). On the basis of the optimized data two plants viz. *Curcuma longa* Linn. and *Zingiber officinale* with an optimization score of more than 5 are most promising as radio-protector

CONCLUSION

Natural radio-protecor possess modulation mechanisms to protect against radiation injuries. Identification of natural lead molecules that are safe food ingredients and appear promising in providing protection against harmful ionizing radiation as studied by *in silico* bio-prospection, is a cost effective way of radio-protector development. Further, *in vitro, in vivo* and preclinical studies on the selected plant products are warranted to reveal the presence of multiple active bioactive ingredients that may be acting in synergism. Furthermore, standardization of extraction procedures for obtaining specific bioactive components, their identification and toxicological studies followed by efficacy testing at different levels of organization of living organisms may lead to development of efficient and safe radio-protective drugs.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest. The research received no specific grant from any funding agency in the public, community, or non-for profit sectors.

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CITATION OF THIS ARTICLE

J R Xavier, O P Chauhan, V Vijay, P E Patki ,R K Sharma*. In silico* modeling for identification of radio protectors of Phyto- and Phyco-origin based on their bioactivity properties. Bull. Env.Pharmacol. Life Sci., Spl Issue [4]: 2022: 239-246