Glutathione-*S*-transferases (GST) catalyze the nucleophilic conjugation of the sulfhydryl group of GSH to the electrophilic centre of various carcinogens, mutagens, xenobiotics etc for their disposition/elimination[16]. Studies demonstrated, reduced GST activity in EAC and fibrosarcoma control mice. *T. dioica* root extracts recuperated the lower hepatic GST activity in carcinoma and fibrosarcoma-affected mice. Thus, GSH and GSTs played their respective roles in the attenuation of oxidative stress, leading to the retardation of tumour progression in mice.

The enzymes are regarded as the first line of endogenous antioxidant defence. Superoxide dismutase (SOD) and catalase (CAT) are the enzymes responsible for catalyzing the disposal of superoxide and hydrogen peroxide (H_2O_2) radicals (ROS) respectively (Fig. 5)[18]. The decline in hepatic SOD and CAT activities was reported in EAC and fibrosarcoma control mice. Treating with TDA and CETD remarkably modulated the SOD and CAT activities in both spheres. Retrieval of endogenous enzymatic activities like GSTs, SOD and CAT; in cancer-affected mice receiving TDA and CETD, showed the fortification of cellular enzymatic antioxidant defence processes through which carcinoma and sarcoma-induced oxidative impact was obviated in rodents.

Different antioxidant natural products have been found to show both pro-oxidant and antioxidant activities[4,24]. It is fascinating to place on record that, TDA exhibited a pro-oxidant effect *in vivo* at larger doses in EAC-bearing mice leading to tumour growth instigation i.e., a totally reverse effect. In the case of the cytotoxic studies *in vitro* against EAC cells, TDA exhibited an inverse relationship with concentration as already discussed above. The biphasic response of TDA both *in vitro* and *in vivo* against EAC needs rigorous further studies.

The *in vitro* free radical scavenging activity of TDA may furnish a ground for its demonstrated antioxidative activity *in vivo* towards the carcimona and sarcoma-affected mice. *In vivo* antioxidant and antigenotoxic effects of *T. dioica* root were also reported against arsenic toxicity in rodents[25-27]. The cytotoxic and antimitotic properties may be the cause for its antitumor activity and the cytotoxic and antitumor effects, on the other hand, may be accountable for its chemopreventive potential, the antioxidant role being the general determinant. All these activities may be responsible for the other reported pharmacological activities like laxative, analgesic, anti-inflammatory, and anthelmintic properties of *T. dioica* root[19,28-31].

Fig. 6 — a) Cucurbitadienol; b) Taraxerol; and c) Colocynthin.

The prevalence of cucurbitacin-type triterpenoid aglycones was ascertained in *T. dioica* root in the research works being discussed by qualitative phytochemical estimation along with high-performance thin layer chromatography (HPTLC)[13,16]. Cucurbitacins (a class of tetracyclic triterpenoids) are reported to bear several beneficial pharmacological effects embracing anticancer effect[32-34]. *T. dioica* root has already been reported to possess specific antitumor triterpenes like cucurbitadienol (Fig. 6a), α-amyrin, ß-amyrin, euphol, lupeol, taraxerol (Fig. 6b) etc. It also has additional antineoplastic constituents viz. cucurbitacin glycoside – colocynthin (Fig. 6c) and a protein trichosanthin[8,9,34]. The occurrence of the foregoing putative active principles could furnish the phytochemical basis for the discussed cytotoxic, antitumor and cancer chemopreventive potential of *T. dioica* root.

Conclusion

The plant kingdom yielded several potential clinically useful antineoplastic agents. *Trichosanthes dioica* (pointed gourd) is a well-utilized and explored Indian traditional medicinal plant. From the present

pre-clinical antineoplastic studies reviewed, it can be inferred that *T. dioica* root possessed marked cytotoxic effect *in vitro*, antimitotic effect *in vitro*, antitumor and cancer chemopreventive actions *in vivo* in mice by means of its inherent antioxidative property mediated by multiple modalities. It may hence be concluded that the *in vitro* cytotoxic, antimitoitic and antioxidant effects of *T. dioica* root together may yield the mechanistic ground for its antitumor and chemopreventive potential *in vivo*. Further chemical and pharmacological investigations on *T. dioica* root in this direction, may furnish newer safe and effective antitumor leads/ drugs from this plant for possible clinical utilization in antineoplastic medication.

Conflict of interest

The author declares no conflicts of interest.

References

1 Tripathi K D, *Essentials of Medical Pharmacology*, (Jaypee Brothers Medical Publishers Pvt. Ltd., New Delhi), 2013.

2 Bennett P N and Brown M J, *Clinical Pharmacology*, (Churchill Livingstone, New Delhi), 2018.

3 Bhattacharya S, Natural antimutagens: A review, *Res J Med Plants*, 2011, **5**(2), 116-126.

4 Bhattacharya S, Vitamin C in cancer management: clinical evidence and involvement of redox role, In *Handbook of oxidative stress and cancer: mechanistic aspects*, 1st edn, edited by S Chakraborti, B K Ray & S Roychowdhury, (Springer, Singapore), 2022, 2421-2433.

5 Bhattacharya S, Medicinal plants and natural products in amelioration of arsenic toxicity: A short review, *Pharm Biol*, 2017, **55**(1), 349-354.

6 Haldar P K, Bhattacharya S, Dewanjee S and Mazumder U K, Chemopreventive efficacy of *Wedelia calendulaceae* against 20-methylcholanthrene-induced carcinogenesis in mice, *Environ Toxicol Pharmacol*, 2011, **31**(1), 10-17.

7 Surh Y J, Cancer chemoprevention with dietary phytochemicals, *Nat Rev Cancer*, 2003, **3**(10), 768-780.

8 Khandaker M, Akter S and Imam M Z, *Trichosanthes dioica* Roxb.: A vegetable with diverse pharmacological properties, *Food Sci Human Wellness*, 2018, **7**(1), 34-48.

9 Islam M T, A literature-based phytochemical evidence and biological activities of *Trichosanthes dioica* Roxb, *Orient Pharm Exp Med*, 2018, **18**, 77-85.

10 Bhattacharya S, Prasanna A and Haldar P K, Evaluation of antiproliferative activity of *Trichosanthes dioica* root against Ehrlich ascites carcinoma cells, *Acad J Cancer Res*, 2011, **4**(2), 38-42.

11 Bhattacharya S and Haldar P K, Evaluation of *in vitro* cytotoxic effect of *Trichosanthes dioica* root, *Pharmacogn Res*, 2010, **2**(6), 355-358.

12 Bhattacharya S and Haldar P K, Evaluation of antimitotic and genotoxic effects of the triterpenoid enriched extract from *Trichosanthes dioica* root, *American-Eurasian J Toxicol Sci*, 2012, **4**, 20-23.

13 Bhattacharya S, Prasanna A, Majumdar P, Kumar R B S and Haldar P K, Antitumor efficacy and amelioration of oxidative stress by *Trichosanthes dioica* root against Ehrlich ascites carcinoma in mice, *Pharm Biol*, 2011, **49**(9), 927-935.

14 Bhattacharya S and Haldar P K, The triterpenoid fraction from *Trichosanthes dioica* root exhibits antiproliferative activity against Ehrlich ascites carcinoma in albino mice: Involvement of possible antioxidant role, *J Exp Therap Oncol*, 2012, **9**(4), 281–290.

15 Bhattacharya S and Haldar P K, *Trichosanthes dioica* root extract induces tumor proliferation and attenuation of antioxidant system in albino mice bearing Ehrlich ascites carcinoma, *Interdiscip Toxicol*, 2011, **4**(4), 184–190.

16 Bhattacharya S and Haldar P K, Chemopreventive property of *Trichosanthes dioica* root against 3-methylcholanthrene-induced carcinogenesis in albino mice, *J Environ Pathol Toxicol Oncol*, 2012, **31**(2), 109-119.

17 Bhattacharya S and Haldar P K, *In vitro* antioxidant activity of *Trichosanthes dioica* root, *J Nat Ayurvedic Med*, 2020, **4**(4), 000279.

18 Haldar P K, Kar B, Bala A, Bhattacharya S and Mazumder U K, Antitumor activity of *Sansevieria roxburghiana* rhizome against Ehrlich ascites carcinoma in mice, *Pharm Biol*, 2010, **48**(12), 1337-1343.

19 Bhattacharya S and Haldar P K, The triterpenoid fraction from *Trichosanthes dioica* root suppresses experimentally induced inflammatory ascites in rats, *Pharm Biol*, 2013, **51**(11), 1477-1479.

20 Das S, Bhattacharya S, Pramanik G and Haldar P K, Antitumour effect of *Diospyros cordifolia* bark on Ehrlich ascites carcinoma-bearing Swiss albino mice, *Nat Prod Res*, 2012, **26**(17), 1631-1633.

21 Bhattacharya S, Protective role of the essential trace elements in the obviation of cadmium toxicity: glimpses of mechanisms, *Biol Trace Elem Res*, 2022, **200**(5), 2239-2246.

22 Bhattacharya S, The Role of *Spirulina* (*Arthrospira*) in the mitigation of heavy-metal toxicity: An appraisal, *J Environ Pathol Toxicol Oncol*, 2020, **39**(2), 149–157.

23 Bhattacharya S, Essential trace metals as countermeasure for lead toxicity, *J Environ Pathol Toxicol Oncol*, 2022, **41**(2), 61-67.

24 Sotler R, Poljšak B, Dahmane R, Jukić T, Jukić D P, *et al.*, Prooxidant activities of antioxidants and their impact on health, *Acta Clin Croat*, 2019, **58**(4), 726–736.

25 Bhattacharya S and Haldar P K, Ameliorative effect *Trichosanthes dioica* root against arsenic-induced brain toxicity in albino rats, *Toxicol Environ Chem*, 2012, **94**(4), 769-778.

26 Bhattacharya S and Haldar P K, Ameliorative effect *Trichosanthes dioica* root against experimentally induced arsenic toxicity in male albino rats, *Environ Toxicol Pharmacol*, 2012, **33**(3), 394-402.

27 Bhattacharya S and Haldar P K, *Trichosanthes dioica* root alleviates arsenic induced myocardial toxicity in rats, *J Environ Pathol Toxicol Oncol*, 2013, **32**(3), 251-261.

28 Bhattacharya S and Haldar P K, Neuropharmacological properties of *Trichosanthes dioica* root, *Chinese J Nat Med*, 2013, **11**(2), 158−163.

29 Bhattacharya S, Haldar P K and Ghosh A K, Paralytic and lethal effects of *Trichosanthes dioica* root extracts in experimental worms, *Pharm Biol*, 2010, **48**(9), 960-965.

30 Bhattacharya S and Haldar P K, *Trichosanthes dioica* root possesses stimulant laxative activity in mice, *Nat Prod Res*, 2012, **26**(10), 952-957.

31 Bhattacharya S and Haldar P K, Protective role of the triterpenoid-enriched extract of *Trichosanthes dioica* root against experimentally induced pain and inflammation in rodents, *Nat Prod Res*, 2012, **26**(24), 2348-2352.

32 Kaushik U, Aeri V and Mir S R, Cucurbitacins – An insight into medicinal leads from nature, *Pharmacogn Rev*, 2015, **9**(17), 12–18.

33 Alghasham A A, Cucurbitacins – a promising target for cancer therapy, *Int J Health Sci (Qassim)*, 2013, **7**(1), 77-89.

34 Mukherjee P K, Singha S, Kar A, Chanda J, Banerjee S, *et al.*, Therapeutic importance of Cucurbitaceae: A medicinally important family, *J Ethnopharmacol*, 2022, **282**, 114599.