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Anticancer activity of cow urine distillate, an update

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Abstract
The prevalence of several threatening diseases such as cancer, chronic ailments, and mental troubles is attributed to the polluted environment and stressed modern lifestyle. According to Indian principles, 'Mother Nature', gave us the gift of the 'cow' as the 'mother of all'. The five principal products derived from the cow are milk, curd, ghee, dung, and urine, which have been consistently employed in Indian culture from ancient times and are together referred to as Panchgavya. Cow products provide both direct and indirect immune-boosting processes that aid in the fight against illnesses and germs, as evidenced by antibacterial, antifungal, and anticancer properties. Cow urine distillate (CUD) has long been used successfully for cancer therapy, as observed in cancer patients. It also has cancer-curing potential in its advanced phases. Its beneficial properties have attracted international attention as a result of patents obtained for its anticancer effects. More time and research are still required to explain the mechanism of action and validation.

Keywords: Panchgavya chikitsa, Holy mother, Cow urine distillate, Anticancer activity

Introduction
Cancer is the uncontrolled cell growth or development of tumor due to the genetic changes in genome that is named as mutation. Being a devastating and leading disease, it poses a major impact on society worldwide. There are almost 10 million deaths per year due to cancer and approximately one out of every six overall deaths. Genomic instability and DNA damage both are the primary cause of cancer. It is not contagious but related to the environment and way of living. Mutation in the cellular genome inactivates the tumor suppressor genes or inactivates the DNA repair system or induce conversion of proto-oncogene to oncogene that lead to unconditional cell proliferation (Ferguson *et al.*, 2015). Physical and chemical agents those are linked to our lifestyle are mainly responsible for induction of cancer e.g. tobacco smoking (lung cancer), asbestos (mesothelioma), alcohol (liver cancer), poor/high salt diet (gastric cancer), high fat diet/obesity (colorectal cancer). Other environmental factors like pathogens e.g. viruses-human papillomavirus (cervical carcinoma), hepatitis B & C (hepatocellular carcinoma); bacteria-*Helicobacter pylori* (gastric carcinoma); parasite-*Schistosomahaematobium* (squamous cell carcinoma of bladder), ionizing and non-ionizing radiations, etc., also contribute significantly in the development of cancer (Anand *et al.*, 2008).

Formation of ROS is the natural phenomenon that occurs inside the body that is generally scavenged by the natural antioxidant system. However, the disturbance in metabolic system i.e. imbalanced formation and scavenging of ROS lead to the oxidative stress. It can also be defined as the excessive production of ROS that exceeds its threshold level inside the cell ultimately affects or damage the key regulatory components of the cellular signalling system. It may also permanently damage the first line defensive compounds like thiols bound protein or non-protein bound sulfhydryl macromolecules that cause the damage in cellular machinery by lipid peroxidation, protein and nucleic acid alterations (Adwas *et al.*, 2019).

ROS formed over time in response to be a long-term environmental stress results in severely damaged cellular structure and functions, as well as to induction of somatic mutations and neoplastic transformation. Indeed, oxidative stress has been linked to cancer onset and progression by raising DNA mutations or causing DNA damage, genetic instability, and cell proliferation. The link between oxidative stress, inflammation and cancer is well reported and confirmed by efficacy of anti-inflammatory treatment therapies for cancer treatment (Reuter *et al.*, 2010). Ayurveda also supported the same with mention of inflammation as a continuous irritation and states that a continuous irritation for long periods can result in development of cancers (Garodia *et al.*, 2007).

Being a constant battle worldwide, development of cures and preventive treatment therapies is continuously progressing. Currently available treatments for cancer are chemotherapy, radiation, and chemically generated medications, which have different associated limitations and side effects. Chemotherapy, for example, can put people under a lot of stress and harm their health. As a result, there is an emphasis on employing alternative cancer treatments and plant/animal based strategies are the most commonly looked alternatives (Greenwell and Rahman, 2015). Plant based compounds and animal peptides are being targeted to develop specific anticancer agents, thus developing a better substitute for cancer prevention and treatment (Wang *et al.*, 2017). Anti-cancer potential of phenolic compounds from dietary and non-dietary natural resources are well explored (Ramos, 2008, Roleira *et al.*, 2015).

Table 1: Different case studies suggesting anticancer activities of cow urine distillate (Dhama *et al.*, 2005)

Type of cancer	Identity	Cowpathy product	Recovery status
Oro-Pharyngeal Carcinoma	Female (63 years old) (Kerala)	Amrutha Sara	Completely recovered
Cancer near the kidney	Mr Kamlesh Kumar Agarwal (MP)	Kamdhenu Ark	98% improvement
Throat cancer	Mr. Ram Sagar Singh (North Bihar)	Kamdhenu Ark	80% improvement
Breast cancer	Smt. SeemaVerma (North Bihar)	Kamdhenu Ark	Completely cured
Chronic renal failure	Mr. Babulal Rungta	Kamdhenu Ark	Improvement
Multiple myeloma and severe waist pain	Mr. Nanak Bhosray Dhingra	Kamdhenu Ark	Improvement

Cow science and anti-cancer strategies/ treatments

In ancient texts of Indian medicinal system and various religious books 'Cow' is revered as a mother figure due to its vitalizing and health promoting products. Cow urine, sometimes termed as 'nectar of god- Amrita' has been described as an effective medicinal substance of animal origin with countless therapeutic benefits in different Ayurvedic texts. It is also an indispensable part of Panchgavya - a combination of five different cow products viz. milk, urine, curd, dung and ghee. Panchgavya as well as the individual products possess medicinal properties and are used to treat different diseases by 'Panchgavya Chikitsa'. Cow urine has been suggested to be beneficial for various ailments such as obesity, diarrhoea, anaemia, edema, jaundice, haemorrhoids and skin diseases. Some evidences of cow urine benefits in cancer treatment are also available.

Dhama *et al.* (2005) reported few case studies related to effect of Re-distillate Cow Urine Distillate (RCUD) as anticancer agent. A female from Kerala with age of 63 years had oropharyngeal carcinoma, who was completely recovered with the intake of Amurtha Sara, made from cow urine. Two other patients, Mr. Kamlesh Kumar from Madhya Pradesh and Mr. Ram Sagar Singh from North Bihar had kidney and throat cancers, respectively, who consumed cow urine preparation named as Kamdhenu Ark and claimed 80-90% recovery. In addition, patients of breast cancer, chronic renal and multiple myeloma felt relieved from the diseases with the intake of Kamdhenu Ark (Table 1).

Upon biochemical analysis, urea (2.1gm %), uric acid (28.05mg %), phenols (43.62 mg %) and amino acid (15.21 mg %) were found in cow ark (Nithya, 2021). Further redistillation of RCUD revealed the presence of benzoic acid, 2-butenedinitrile furanonitrileisovaleric acid, acetic acid phenyl trimethylsilyl and propionic acid (US 7718360, Chakrabarti *et al.*, 2010). This phenolics rich composition of cow urine distillate might be responsible for observed beneficial effects upon consumption by cancer patients. There are also different patents available related to anticancer activity of cow urine- US 6410059-B1 (Khanuja *et al.*, 2002), EP 1330253 B1 (Khanuja *et al.*, 2004), US 7235262 (Khanuja *et al.*, 2007) and US 7718360 (Chakrabarti *et al.*, 2010). Patents by Khanuja *et al.* were on the use of bioactive fraction from cow urine distillate (Go Mutra) as a bio-enhancer of anti-infective, anti-cancer agents and nutrients. These patents suggest that intake of cow urine along with prescribed allopathic medicines enhance the efficacy of drugs and speed of recovery from underlying infectious and cancerous diseases. The patent from Chakrabarti *et al.* 2010 claimed that RCUD composition prevent or protect the DNA from damage induced by oxidative stress. A detailed composition of RCUD and stepwise method for accessing the damaged DNA after RCUD treatment was described in this patent.

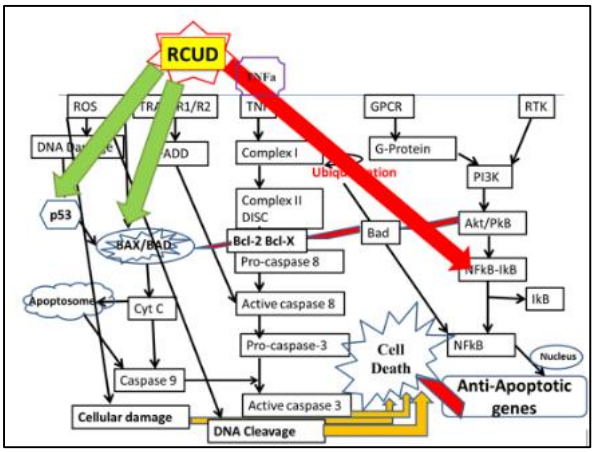

Fig. 1: The possible mechanism of action of RCUD on apoptotic and anti-apoptotic pathways. Action of RCUD represented by green and red arrows that showed the activation and inhibition of proteins involved in apoptotic and anti-apoptotic pathways, respectively.

Proposed mechanism of action

In normal cellular machinery, ~1.5 x 10^5 oxidative hits per day occurs in each cell, driving factor of which are ROS. When proportion of ROS increases than the ROS scavenged by anti-oxidative system, oxidative stress hits the cells, which is implicated in cancer pathophysiology. Under normal conditions ROS regulate various pathways such as JNK/ p38 MAPK, PI3K/Akt, p53 induced cell cycle regulation, Nf-kB signalling and apoptotic pathways (Fig. 1).In state of aging or dysfunction, the ultimate fate of a normal cell is apoptotic cell death via caspase dependent and independent pathways. DNA damage or other irregularity due to oxidative stress in cell is detected by cell cycle checkpoints, which directs the cell towards apoptosis. However, under prolonged oxidative stress, during the cell division, cell breaches these cell cycle checkpoints (G1/S and G2/M) and results in uncontrolled cell proliferation (Singhal *et al.*, 2005) (Fig. 2). Oxidative stress affect PI3K/Akt, Nf-kB and BCl-2 pathways of apoptosis/cell survival leads to upregulation of anti-apoptotic genes and inhibits the cell death. RCUD might be exerting its beneficial anticancer effect via modulating the expression of p53 and

reinstating the cell cycle regulatory check points as well as suppressing the expression of anti-apoptotic proteins via BAX-BAD, PI3K/Akt (Kwon *et al.*, 2007, Fresco *et al.*, 2010, Liu *et al.*, 2017) and NF-kB pathway regulation (Fig. 1).

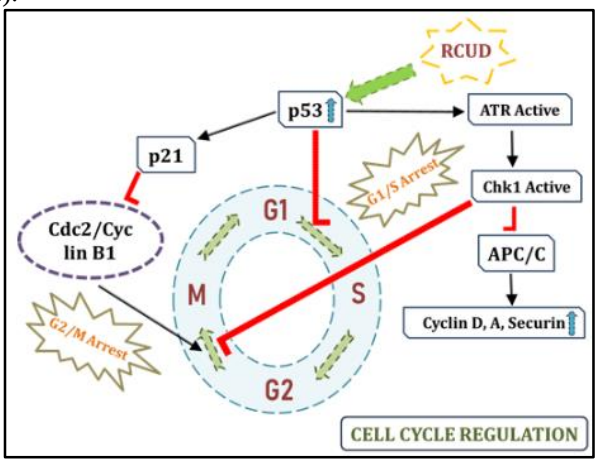

Fig. 2: The possible mechanism of action of RCUD on cell cycle regulation. RCUD might increase the expression of p53 protein that regulates the cell cycle with G1/S and G2/M arrest.

The proposed mechanism of action is based on the revealed cow urine composition upon biochemical and redistillation analysis. Phenolics were the major compounds which could be responsible for anticancer activity. Dietary and non-dietary phenols have been well reported to possess anticancer activity and modulating the aforesaid mechanisms. A number of studies showed the evidences regarding the effect of phenols on the regulatory proteins of signalling pathways that ultimately leads to apoptosis (Ramos 2008, Mathan *et al.*, 2016). However more studies are required to link the anticancer potential and hypothesized mechanism of action of cow urine.

Conclusion and future perspectives

"Panchgavya chikitsa' or 'Cowpathy' or 'Cow science' offers a new sector as a complementary/alternative medicine for cancer treatment with available preliminary evidences. Cow urine based compositions possess anticancer activities which are supported by patents granted and reported case studies. The hypothesized mechanism is based on previous literature reports suggesting the pathways being modulated by other phenolic compounds with anticancer potential. Further, extensive studies are required, where the possible bioactive compounds can be isolated and used to validate the hypothesized mechanism of action with standard analytical compounds.

Source of Funding

None.

Conflict of Interest

None.

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