



Chemotherapeutic potential of cow urine: A review

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ABSTRACT

In the grim scenario where presently about 70% of pathogenic bacteria are resistant to at least one of the drugs for the treatment, cue is to be taken from traditional/indigenous medicine to tackle it urgently. The Indian traditional knowledge emanates from ayurveda, where *Bos indicus* is placed at a high pedestal for numerous uses of its various products. Urine is one of the products of a cow with many benefits and without toxicity. Various studies have found good antimicrobial activity of cow's urine (CU) comparable with standard drugs such as ofloxacin, cefpodoxime, and gentamycin, against a vast number of pathogenic bacteria, more so against Gram-positive than negative bacteria. Interestingly antimicrobial activity has also been found against some resistant strains such as multidrug-resistant (MDR) *Escherichia coli* and *Klebsiella pneumoniae*. Antimicrobial action is enhanced still further by it being an immune-enhancer and bioenhancer of some antibiotic drugs. Antifungal activity was comparable to amphotericin B. CU also has anthelmintic and antineoplastic action. CU has, in addition, antioxidant properties, and it can prevent the damage to DNA caused by the environmental stress. In the management of infectious diseases, CU can be used alone or as an adjunctive to prevent the development of resistance and enhance the effect of standard antibiotics.

KEY WORDS: Antibiotic, antifungal, antineoplastic, bioenhancer, *Bos indicus*, immune-enhancer

INTRODUCTION

Infectious diseases remain a major threat to the public health despite tremendous progress in human medicine. Emergence of widespread drug resistance to the currently available antimicrobials is a matter of deep concern. A high percentage of nosocomial infections are caused by highly resistant bacteria such as methicillin-resistant *Staphylococcus aureus* or multidrug-resistant (MDR) Gram-negative bacteria. Each year in the United States, about 2 million people become infected with antibiotic resistant bacteria and at least 23,000 people die every year as a consequence of these infections. Many more people die from other conditions that are complicated by an antibiotic-resistant infection [1]. In 2012, there were about 450000 new cases of MDR tuberculosis. Extensively drug-resistant tuberculosis has been identified in 92 countries. Development of resistance to oral drug of choice fluoroquinolones, for urinary tract infections caused by *Escherichia coli* is very widespread, often sensitivity remains only for injectables [2]. Infections caused by resistant microorganisms often fail to respond to the standard treatment, resulting in prolonged illness, higher health care expenditures, and a greater risk of death. There is a dire need for the development of new antimicrobial agents with sensitivity intact against microorganisms [3,4]. The rational designing of novel drugs from traditional medicines to treat

these difficult to treat infections offers a new prospect for the modern health-care system.

Ayurvedic texts (Sushruta Samhita, Ashtanga Sangraha and Bhav Prakash Nighantu) describe cow urine (CU) (gomutra) as an effective medicinal substance/secretion of animal origin with innumerable therapeutic uses. Cow (Kamadhenu) has been considered as a sacred animal in India. In Rigveda (10/15), CU is compared to nectar. In Susruta (45/221) and in Charak (sloka-100) several medicinal properties of CU have been mentioned such as weight loss, reversal of certain cardiac and renal diseases, indigestion, stomach ache, diarrhea, edema, jaundice, anemia, hemorrhoids and skin diseases including vitiligo. Gomutra is capable of removing all the imbalances in the body, thus maintaining the general health [5]. CU contains 95% water, 2.5% urea, minerals, 24 types of salts, hormones, and 2.5% enzymes. It also contains iron, calcium, phosphorus, carbonic acid, potash, nitrogen, ammonia, manganese, iron, sulfur, phosphates, potassium, urea, uric acid, amino acids, enzymes, cytokine and lactose [6].

CU is an effective antibacterial agent against a broad spectrum of Gram-negative and Gram-positive bacteria and also against some drug-resistant bacteria. It acts as a bio-enhancer of some antimicrobial drugs. It has antifungal, anthelmintic, antineoplastic action, is useful in hypersensitivity reactions and

in numerous other diseases including increasing the life-span of a person. Recent researches have shown that CU is an immune-enhancer also [7-9]. Therapeutic properties of CU have been validated by modern science also.

MECHANISM OF ACTION OF CU

Different fractions of CU possess antimicrobial activity due to the presence of certain components like volatile and nonvolatile ones [10-13]. Presence of urea, creatinine, swarn kshar (aurum hydroxide), carbolic acid, phenols, calcium, and manganese has strongly explained the antimicrobial and germicidal properties of CU [14-16]. Presence of amino acids and urinary peptides may enhance the bactericidal effect [17] by increasing the bacterial cell surface hydrophobicity. CU enhances the phagocytic activity of macrophages. Higher amounts of phenols in fresh CU than CU distillate (CUD) makes it more effective against microbes.

After photo-activation, few biogenic volatile inorganic and organic compounds such as CO₂, NH₃, CH₄, methanol, propanol and acetone, and some metabolic secondary nitrogenous products are also formed [18]. Photo-activated CU (PhCU) becomes highly acidic in comparison to fresh CU. An increase in bactericidal action may be due to a significant decrease in pH [12], presence of inorganic phosphorus, chloride and dimethylamine may also play an important role [19], along with increased formation of some reactive compounds like formaldehyde, sulfinol, ketones and some amines during photo-activation and long term storage [20]. CU prevents the development of antibacterial resistance by blocking the R-factor, a part of plasmid genome of bacteria [21].

CU contains phenolic acids (gallic, caffeic, ferulic, o-coumaric, cinnamic, and salicylic acids) which have antifungal characteristics [22].

Antioxidant property of uric acid and allantoin present in CU correlates with its anticancer effect. CU reduces apoptosis in lymphocytes and helps them to survive better [5]. This action may be due to the free radical scavenging activity of the urine components, and these components may prevent the process of aging [10]. It efficiently repairs the damaged DNA [5].

Daily consumption of CU improves immunity due to the presence of swarn kshar and fastens the wound healing process, which is due to allantoin [8]. CU enhances the immunocompetence by facilitating the synthesis of interleukin-1 and -2 [23,24], augments B- and T- lymphocyte blastogenesis, and IgA, IgM and IgG antibody titers [25].

Early morning first voided CU is more sterile and have more macro and micronutrients along with other enzyme/urea content could be more effective [26].

AS ANTIMICROBIAL AGENT

Antimicrobial activity of CU from both indigenous and hybrid breeds against *E. coli*, *Salmonella typhi*, *Proteus vulgaris*,

S. aureus, *Bacillus cereus*, *Staphylococcus epidermidis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Pseudomonas fragi*, *Streptococcus agalactiae*, *Enterobacter aerogenes*, *Aeromonas hydrophila*, *Micrococcus luteus*, *Streptococcus pyogenes*, *Streptomyces aureofaciens*, *Lactobacillus acidophilus* and *Bacillus subtilis*, and *Leishmania donovani* has been observed in various studies. In these studies the antimicrobial activity of CU was found to be comparable with ofloxacin, ciprofloxacin, ampicillin, chloramphenicol, nalidixic acid, rifampicin, tetracycline, streptomycin, cefpodoxime and gentamycin in different studies [27-36].

Studies with Indigenous *Bos indicus* Breeds of Cow

Fresh CU (FCU), Sterile, PhCU and CUD from a healthy Geer cow, was used to assess the antibacterial effect against different strains of bacteria. Against *E. coli*, FCU had the bigger mean of inhibition zone (15 mm) than Sterile, PhCU, and CUD (~10 mm). FCU had good activity of 15, 16 and 20 mm of inhibition against *E. coli*, *B. subtilis*, and *S. typhi*, respectively. Other forms of CU showed activity against *E. coli*, *S. typhi*, *P. vulgaris*, *S. aureus* and *B. subtilis* [27].

Rana and De [28] observed a greater activity against Gram-positive than Gram-negative bacteria with CU obtained from Geer cow. The minimum inhibitory concentration (MIC) in all the four tested Gram-positive bacteria was 134 mg/ml. Among Gram-negative organisms, *P. aeruginosa* was more sensitive (MIC 134 mg/ml) than *P. vulgaris* (MIC 268 mg/ml). Mean zone of inhibition (mm) \pm standard error of the mean against *B. subtilis* was found to be 18.67 ± 1.15 , which was less than 27 for Gentamycin 10 mcg and cefpodoxime 10 mcg. Activity (18.67 ± 1.15) against *B. cereus* and was similar to that of cefpodoxime (19) but less than with gentamycin (26). Activity (16) against *S. aureus* and *S. epidermidis* was <25 for Gentamycin and ~23 with Cefpodoxime. No inhibition against *P. aeruginosa* was observed with Cefpodoxime while CU had an inhibition of 19.33 ± 1.15 mm and Gentamycin 35 mm. Against *P. vulgaris* inhibition was comparable between CU (16 ± 1.73), gentamycin (21) and cefpodoxime (20). There was comparable inhibition of *P. vulagris* by CU (16 ± 1.73), gentamycin (21) and cefpodoxime (20). Against *K. pneumoniae*, inhibition observed with CU (15.67 ± 0.57) was less than gentamycin (34) and cefpodoxime (20).

Comparatively FCU obtained from Gujarati Geer cow was found to have more antimicrobial activity than its distillate (Table 1).

Similar findings were reported by Jarald *et al.* [29]. Mean zone of inhibition (mm), using Sahiwal CUD, was found to be 19.2 for *S. aureus*, 20.2 for *P. fragi*, 18.8 for *E. coli*, 23 for *B. subtilis*, 19 for *S. agalactiae* and 17 for *P. vulgaris*. There was a progressive decrease in optical density (indicator of antimicrobial activity and was measured by spectrophotometer at 600 nm) over 5 h when FCU was added to the respective inoculums [29].

The antibacterial efficacy (as mean zone of inhibition in mm) of CU Concentrate (CUC) obtained from Karnataka breed, Amrit

Table 1: Antimicrobial activity of CU, CUD (Gujrati Geer cow) in comparison to standard drug Ofloxacin [10]

| | <i>E. coli</i> | <i>S. epidermidis</i> | <i>S. aureus</i> | <i>K. pneumoniae</i> | <i>P. vulgaris</i> | <i>B. subtilis</i> |
|-----------|----------------|-----------------------|------------------|----------------------|--------------------|--------------------|
| FCU | 23 | 22 | 24 | 25 | 23 | 24 |
| CUD | 20 | 20 | 18 | 20 | 20 | 21 |
| Ofloxacin | 30 | 28 | 25 | 28 | 28 | 32 |

E. coli: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *P. vulgaris*: *Proteus vulgaris*, *B. subtilis*: *Bacillus subtilis*, *S. epidermidis*: *Staphylococcus epidermidis*, FCU: Fresh cow urine, CUD: Cow urine distillate, CU: Cow urine

mahal was comparable with Streptomycin on *B subtilis* (16:18), *S. aureus* (16:19), *E. coli* (14:18) and *E. aerogenes* (15:18) using Disc diffusion method [30].

In an *in vitro* study, 30 µL of PhCU of Haryana breed was found to be comparable in efficacy to Tetracycline (30 µg mL). Antimicrobial activity (mean zone of inhibition in mm) of PhCU and Tetracycline, respectively against *B. cereus* was 17 and 22, *S. aureus* was 18 and 21, *S. typhimurium* was 21 and 22, *A. hydrophila* was 22 and 24, *E. aerogenes* was 13 and 18 and *M. luteus* was 15 and 17 [31]. Similar results were found in another study with PhCU of Haryana breed against these bacteria [32].

Studies where breed of cow is not mentioned

In an *in-vitro* test, activity of FCU was comparable to Streptomycin. Similar mean zone of inhibition (mm) was seen against gram positive organisms *E. coli* (16:16:13), *K. pneumoniae* (15:17:12) and *P. aeruginosa* (17:19:15) with FCU and Streptomycin and lesser with PhCU (by keeping urine in sunlight in sealed glass bottles for 72 h), respectively. Comparatively lesser antibacterial activity against gram negative organisms *S. aureus* (18:26:17), coagulase negative *Staphylococci* (18:29:15), *B. subtilis* (20:29:15), and *S. pyogenes* (20:26:14) was seen for FCU than streptomycin, and still lesser than with PhCU [33]. No antibacterial activity was seen for CUD, which is contradictory to some previous reports [34].

Vats *et al.* [35] studied the synergistic antimicrobial effect of PhCU and herbs against bacterial and fungal strains. PhCU and *Azadirachta indica* combination showed a remarkable synergistic antimicrobial activity against *Candida tropicalis*, *Candida glabrata*, *P. aeruginosa*, and *S. aureofaciens*. PhCU and *Terminalia chebula* showed maximum activity against *S. aureofaciens* (45 mm), and *P. aeruginosa* (zone of inhibition of 40 mm). *Piper nigrum*, *T. chebula* and PhCU in combination were most effective against *C. glabrata* (35 mm) and *C. tropicalis* (45) mm.

Upadhyay *et al.* [18] found in *in-vitro* tests that PhCU has better bactericidal activity against *S. aureus*, *B. cereus*, *L. acidophilus*, *M. luteus*, *K. pneumoniae*, *S. pneumoniae* and *E. coli*, when compared with Tetracycline, Ampicillin and Ciprofloxacin. PhCU showed MIC value of 0.25 µl/ml against *S. aureus*, *B. cereus*, *L. acidophilus* and *M. luteus*, while it was found to be 0.125 µl/ml against *E. coli*, which was less than that for antibiotics. A combination of CU with Neem (*A. indica*) oil and Bavchi (*Psoralea coryfolia*) oil showed a synergistic effect (MIC 0.125-0.25 µl/ml), which was less than that for antibiotics. Neem

oil and CU showed 33-35 mm inhibition zones against *B. cereus*, *L. acidophilus*, *M. luteus*, *K. pneumoniae* and *S. pneumoniae*.

Sathasivam *et al.* reported the antibacterial activity of CUD (5, 10 and 15 µl) against the *B. subtilis*, *P. aeruginosa*, *K. pneumoniae* and *S. typhi*. Antibacterial activity (mean zone of inhibition in mm) was observed against *B. subtilis* (7.6 ± 0.04, 8.6 ± 0.17, 8.8 ± 0.17, respectively) *P. aeruginosa* (12.6 ± 0.04, 13.6 ± 0.17, 15.4 ± 1.23, respectively) and *S. typhi* (12 ± 1.23, 13.6 ± 0.17, 15.4 ± 1.23, respectively). This antibacterial activity was more than the positive control of ampicillin (30 mg/disc), which was 7.1 ± 0.01 mm against *B. subtilis*, 11.2 ± 0.01 mm against *P. aeruginosa* and 9.6 ± 0.02 mm of inhibition zone against *S. typhi*. Antibacterial activity against *K. pneumoniae* was 11 ± 0.14 mm with 15 µl of CUD, which was more than the activity (9.5 ± 0.05 mm) with Ampicillin [34].

Yadav *et al.* reported the antimicrobial property of a herbal formulation containing CU, *Dalbergia sissoo*, and *Datura stramonium*. The antimicrobial activity of CU alone was also found to be significant ($P > 0.001$). It was found that CU extract showed the highest inhibition in gram-positive *S. aureus* (CI, 213%) and comparable activity in *S. pneumoniae* (95%) compared to chloramphenicol (30 µg), nalidixic acid (10 µg), rifampicin (30 µg), and ampicillin (10 µg). In gram-negative bacteria all antibiotics were inactive, except chloramphenicol (30 µg), while CU extract showed significant ($P < 0.05$) activity (35% and 37%, respectively) against *E. coli* and *K. pneumoniae* as compared to Chloramphenicol [36].

CU has anti-*Leishmania donovani* effect (Kala-azar) in an *in-vitro* study [37]. This fact can be further validated by more intensive studies.

PREVENTION OF ANTIBIOTIC RESISTANCE

Pathogenic bacteria are remarkably resilient and have developed several ways to resist antimicrobial drugs. Due to increasing use and rampant misuse of existing antibiotics in human and veterinary medicine, and also in agriculture, threat from antimicrobial resistance is increasing. Resistant strains like Penicillin- and Methicillin- resistant *S. aureus*, vancomycin resistant *Enterococcus*, and ciprofloxacin resistance *P. aeruginosa* are an ever increasing global threat. After photoactivation and purification, CU has been found to be effective against certain drug resistant bacterial strains [38]. CU extract of *A. indica* showed better MIC values than the organic fractions for MDR *E. coli* (12.68 mm) and *K. pneumoniae* (9 mm). CU extracts of *A. indica* showed >8.66 mm zone of inhibition for MDR *S. aureus*, *P. aeruginosa* and *P. vulgaris* [39].

FUNGICIDE AND BIOFUNGICIDE

Fungicidal effect against *Aspergillus fumigatus*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus*, *Malassezia*, *C. tropicalis* and *C. glabrata* has been observed in various studies. CU was highly stable and capable in inhibiting the growth of *Malassezia* fungi (90-95%) responsible for causing dandruff for a longer time (4-5 days), than rice water (due to *B. cereus* growth in rice water) which was stably capable of inhibiting 85-90% of the growth for 3-4 days. Neem leaves extract and Lemon Juice extract were comparatively less effective in this study [40].

15% CU was most active against *Aspergillus*, *Rhizopus* and the percentage of inhibition obtained with it was 85% [41]. 5% CUC showed maximum antifungal activity against *A. niger* (93%), followed by *A. oryzae* (92.67%) and *A. flavus* (83%) [30]. CUD showed better antifungal activity against *A. fumigatus* and *C. albicans* with mean zone of inhibition of 13 and 11 mm than PhCU [27]. More fungal growth suppression (as mm in diameter) was observed with CUD in *A. niger* (8 ± 0.14 , 11.3 ± 1.2 and 12.6 ± 0.04 , respectively) than *A. flavus* (7.3 ± 0.25 , 10 ± 0.26 and 11 ± 1.2 , respectively) with the use of 5, 10 and 15 μ l of CUD [34].

In vitro antifungal activity (in mm) of Geer CU against *A. flavus* (17.33 ± 0.57) was in between 50 μ g of amphotericin B (15) and 10 μ g of clotrimazole (24) and against *C. albicans*, activity was similar with CU (18.67 ± 1.15) and amphotericin B (19), but less than clotrimazole (30) [28]. Antifungal activity of Geer CU is better than the others where source of CU is not mentioned.

In an *in vitro* study, it was found that the urine samples of outdoor feeding cow (OCU) was more effective and inhibited growth of fungi more strongly as compared to indoor feeding CU (ICU). This inhibition was concentration dependent. No growth of *Penicillium notatum*, *Trichoderma viridae*, and *Alternaria solanii* was observed with 10% OCU and with 20% ICU and that of *Claviceps purpurea*, *Rhizopus oligosporius*, *C. albicans* and *A. candidus*, no growth was observed with 20% of OCU only [42].

ANTISEPTIC

Sanganal *et al.* observed the enhanced wound healing activity of CU in Wistar albino rats [43]. On 4th day, the external application of CU showed significant and progressive increase in wound healing in rats compared to different concentrations of CU and 1% w/w nitrofurazone ointment locally. Similar findings were also observed by Maheshwary *et al.* [44].

ANTHELMINTIC ACTIVITY

CUC was found to be more effective than piperazine citrate as anthelmintic agent at both 1% and 5% concentrations. For anthelmintic activity, adult Indian earthworm *Pheretima posthuma* was studied due to its anatomical and physiological resemblance with the intestinal roundworm parasite of human

beings. Paralysis of earthworm occurred in 53 and 48 min with 1% piperazine and CUC, respectively and 16 and 13 min with 5% piperazine and CUC, respectively. Time taken for the death of earthworms decreased from 72 min with 1% piperazine to 60 min with 1% CUC, respectively. It further decreased from 28 min with 5% piperazine to 18 min with 5% CUC, respectively [30].

Different compositions of Panchgavya (five products of cow namely milk, curd, ghee, urine and dung) alone and combination of Panchgavya and ethanolic extract of *Bauhinia variegata* Linn (10%, 50%, 75% in Panchgavya) were found to have excellent anthelmintic activity against adult Indian earthworm (*P. posthuma*) when we compared to control Piperazine (50 and 100 mg/ml). In combination, the anthelmintic activity was synergistic and with increasing doses, time (in minutes) of onset of paralysis and death in earthworm decreased [45].

BIOENHANCER

A 'bioenhancer'/'biopotentiator' is an agent capable of enhancing the bioavailability and efficacy of a drug with which it is co-administered, without any pharmacological activity of its own at the therapeutic dose used. In ayurveda, this concept is known as 'yogvahi' and is used to increase the effect of medicines by increasing the oral bioavailability (especially of medicines with poor oral bioavailability), decreasing their dose and adverse effects, and were used to circumvent the parental routes of drug administration. We can develop more such useful and economically viable drug combinations, by integrating the knowledge of time tested ayurveda with modern methods of research [8]. CU is the only agent of animal origin which acts as bioenhancer of antimicrobial, antifungal, and anticancer agents [30]. The indigenous CU contains 'Rasayana' tatva, which is responsible for modulation of the immune system and also act as a bioenhancer [21].

CUD is more effective bioenhancer than CU [30,46]. CUD enhances the transport of antibiotics like rifampicin, tetracycline and ampicillin across the gut wall by 2-7 folds [47]. It also enhances the potency of taxol against MCF-7 cell lines [48]. It enhances the bioavailability of rifampicin by 80 fold in 0.05 microgm/ml concentrations, ampicillin by 11.6 fold in 0.05 μ g/ml concentrations and clotrimazole by 5 fold in 0.88 μ g/ml concentration [49]. The activity of rifampicin increases by about 5-7 folds against *E. coli* and 3-11 folds against Gram-positive bacteria, when used along with CU [50]. Potency of paclitaxel has been observed to increase against MCF-7, a human breast cancer cell line in *in-vitro* assays [49]. The bioenhancing ability is by facilitating the absorption of drugs across the cell membrane. The CU has been granted US Patents for its medicinal properties, particularly as a bioenhancer along with antibiotics, antifungal and anticancer drugs (6896907, 6410059).

CUD alone caused more inhibition of Gram-positive bacteria. Inhibition caused by streptomycin (1 mg/ml) alone was higher (31-34 mm) than that of CUD alone (19-22 mm). With the

combination of *Pinguicula longifolia*, CUD and streptomycin together, *S. aureus* was inhibited to a more extent (38 mm) followed by *P. aeruginosa* (37 mm) and an equal inhibition was exhibited by *B. subtilis* and *E. coli* (36 mm) [51]. *S. aureus* and *P. aeruginosa* have been recognized as most common bacteria, which have developed resistance against several antibiotics and is a major hospital borne pathogen, which is particularly dangerous to immunocompromised patients. This study is of importance in this scenario.

This bioenhancing activity of CU has been aptly and widely used in various ayurvedic formulations. It is one of the constituents of Hingwadh ghrita, Lashunadh ghrita, Sidhartak ghrita for psychiatric illness used in abdominal tumors and in other formulations like Mandurvatak, Darvi ghrita, and Punnarvamandur. CU is used as yogvahi along with Hareetakyadi yog, Swarnkshiryad yog, Swarmakshik bhasma and Gvakshyadi churana. These preparations are commercially available in the Indian market. Ghritas are available as semisolid preparations while bhasms, yogs, and churans are in the powder form.

ANTICANCER PROPERTIES

CU has antioxidant properties and is a free radical scavenger, and thus it neutralizes the oxidative stress. Scientists proved that the pesticides even at very low doses cause apoptosis of lymphocytes and tissues through fragmentation of DNA while CU helps the lymphocytes to survive by inhibiting their apoptosis and by repairing the damaged DNA and is, therefore, effective as anti-cancer therapy [52,53].

Chemopreventive potential of CU was observed in a study, which was conducted on 70 Swiss albino mice for 16 weeks. Papillomas were induced by 7, 12 dimethyl benzanthracene and later promoted by repeated application of croton oil. In mice treated with CU, the incidence of tumor (papillomas), tumor yield, and its burden was statistically less than the untreated group [54].

Jain *et al.* studied the effect of CU therapy on various types of cancers in Mandsaur area. The severity of symptoms (pain, inflammation, burning sensation, difficulty in swallowing, and irritation) decreased from day 1 to day 8 with CU therapy. Percent of patients with severe symptoms decreased from 82.16 to 7.9 on day 8, patients with moderate symptoms increased from 15.8 to 55.3 and with mild symptoms, patients increased from 1.58 to 36.34. The severity of symptoms decreased further with continued CU therapy [15].

Dutta *et al.* reported the anti-clastogenic and anti-genotoxic effect of redistilled CUD (RCUD) in human peripheral lymphocytes, which have been challenged with manganese dioxide (MnO₂) and hexavalent chromium (Cr+6). Protection in number of chromosomal aberrations and frequency of micronuclei were more prominent when these cells were pretreated with CU than simultaneous treatment with CU [55].

IMMUNOSTIMULANT

The use of herbs and minerals (like chavanprash and panchgavya) for improving the overall resistance of the body against common infections and pathogens has been a guiding principal of Ayurveda. Ancient books on Ayurveda state that consuming CU daily increases the resistance to diseases by up to 104%. CU enhances the humoral, and cell-mediated immune response in mice [5]. CUD was found to augment B- and T-lymphocyte blastogenesis; IgG, IgA and IgM antibody titers in mice. It has been observed that CU also increases the phagocytic activity of macrophages and is thus helpful in the prevention and control of bacterial infections. The level of both interleukins -1 and -2 in mice was increased by 30.9% and 11.0%, respectively, and in rats these levels were increased significantly by 14.75% and 33.6%, respectively [52]. CUD has been reported to be a potent and safe immunomodulator, which increases both humoral, and cell-mediated immunity in mice.

Cell-mediated immune response was evaluated on various parameters in a study by Verma *et al.* using CU for 30 days. There was a 55% increase in phagocytic index, and a significant increase (16%) in neutrophil adhesion on regular use of whole freeze dried CU. CU has the potential to boost the immune functions by increasing the white blood cells counts and subsequently reducing the red blood cells count to a certain extent [56].

Traditional uses of CU

Some of the traditional uses of CU are in fever, where CU along with pepper, curd and ghee is used; in leprosy, CU is used along with dhruhardi and in deformities associated with leprosy, it is used with Nimbuchal, whereas in chronic leprosy, CU is used along with leaves of Vasaka and kanar, and bark of kuraila and neem [11]. Local traditional healers in Mandsaur prescribe CU for worm infestations, to develop immunity and to avoid aging. They suggest 10-25 ml of CU to be taken on an empty stomach for the same [15].

CONCLUSIONS

On analyzing the effect of different preparations of CU, FCU had better activity than CUD [27-32]. Activity of FCU and CUD from indigenous cows was similar to streptomycin and tetracycline. Ayurveda also mentions that FCU of indigenous cows' is the best.

More well-planned studies in human subjects are required to fully assess its potential as an effective antimicrobial agent as most of the studies quoted are *in vitro* studies. Comparative studies between CU obtained from indigenous breeds and of inbred strains may be undertaken, as ayurveda was written when inbred strains of cows were not present. Future development of newer drugs can involve CU in its repository.

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