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Research

Formulation, Evaluation, Pack design & Commercialization of Chlorine Dioxide Gas for Disinfection & Chlorine Dioxide Tablet for Water Treatment

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Abstract

In this research, we have explored and realized safe and effective utility of Chlorine Dioxide gas as a means for disinfection and Chlorine Dioxide Tablet for Water treatment. For generation of Chlorine Dioxide gas, a suitable reactant mixture was formulated. The reactant mixture composition and the extent of gaseous Chlorine Dioxide generation were suitably optimized. Sodium Chlorite and Anhydrous Citric Acid as reactant mixture in the ratio of 9.02:0.98 / 20.8 g: 2.2 g was finalized which produced about 2500 ppm of Chlorine Dioxide gas for effective disinfection of 250 square feet of area. For testing thedisinfectant efficiency, a simple but efficient chemical and microbial evaluation method were designed and utilized. Apart from formulation and evaluation, a suitable pack for the reactant mixture was designed and fabricated so that the contents remain intact and stable during storage and active enough to produce Chlorine Dioxide gas when put to use. The formulated product was found to be stable in the intended packing configuration. The product was successfully commercialized at an affordable price under the brand name CAIR®. Also in this research for Water treatment purpose, Acidulated Chlorine Dioxide Effervescent tablets were formulated by direct blending and compression process. Physico-chemical evaluation was done for the formulated tablets. One (1) tablet produced 0.8 mg / L of Chlorine Dioxide gas sufficient enough to treat about 1 Litre of Water free of pathogens, spores, parasites & cysts. A suitable pack was designed and stability tested to ensure the product remains stable while handling and storage. The product was successfully commercialized at an affordable price under the brand name JAL4AL®.

Keywords: Disinfection, Sterilization, Fumigation, Decontamination

INTRODUCTION

Disinfectants are used to decontaminate by eliminating the microorganisms. Disinfectants act by inhibiting the growth of microorganisms or having lethal action on them. Disinfectants can be divided into oxidizing and non-oxidizing type [1]. The mechanism of disinfectionof Chlorine Dioxide is by oxidation.Chlorine Dioxide inactivates most waterborne pathogens including Cryptosporidium parvum oocysts, spores of pathogen, parasites and cysts of parasites [2]. It is also used to overcome taste and odour problems in potable water [3]. Chlorine Dioxide is a potent Virucidal, Bactericidal, Sporicidal and Fungicidal oxidising agent, with two and a half times the oxidising power of chlorine [4-5].

Chlorine Dioxide has been used for the decontamination of large buildings, such as during the US anthrax outbreak in 2001 (American Media Inc., Boca Raton, FL, USA and the US Department of Justice mail facility in Landover, MD, USA) and to control the presence of moulds in buildings that presented a public health risk following the devastation caused by Hurricane Katrina in New Orleans (LA, USA). Large building decontamination is very different from ward decontamination: A. Bennett, personal communication revealedthe decontamination of a hospital in Oxnard (CA, USA) that was contaminated with mould required the entire building was covered with a large tarpaulin and then fumigated for 24 h with Chlorine Dioxide, at a cost of $25 million.Chlorine Dioxide killsmicroorganisms byaffectingmetabolic enzymes and membrane proteins [6-7]. Chlorine Dioxide is an oxidizing biocide effective in controlling both legionella and biofilm growth in hot and cold water systems. Chlorine Dioxide is not affected by the pH or hardness of the water and has been used for many years in numerous large-scale disinfection applications. Chlorine Dioxide destroys sulfides, cyanides, phenols, controls algae, and neutralizes iron and manganese ions. It is an effective biocide at concentrations as low as 0.1 ppm (parts per million) and over a wide pH range. Unlike iodine, Chlorine Dioxide has no adverse effects on thyroid function. The by-product of Chlorine Dioxide reaction is Chlorite, which is harmless to humans. Unlike chlorine, it does not lead to the formation of trihalomethanes or combine with ammonia to form chlorinated organic products (Chloramines) [8-10].

Chlorine Dioxide is not mutagenic or carcinogenic in humans and was found effective for the sterilization of medical products, the process is relatively rapid (1.5–3 h) and there is little or no need for post-sterilization clean-up activity [11]. Chlorine Dioxide based products like mouth wash, mouth rinse, are effective in improving the overall oral hygiene, helps in the reduction of plaques etc. Chlorine Dioxide also helps in the faster healing of gum damage and post-operative recovery [12-16].In countries like USA, UK and Europe, Chlorine Dioxide is preferred a) for decontamination of animal husbandries, livestock farms, dairy farms, small animal farms, poultries, fisheries etc to prevent animals, avians & aquatic species from getting infection due to disease causing pathogens. b) for disinfection of sewage lines c) for treatment of drinking water lines d) for washing, cleaning & removal of insecticide and pesticide in vegetables & fruits products [17-19].In a multi specialty hospital - American University Medical Center-Rizk Hospital based in Lebanon, a study was conducted on the efficiency of Chlorine Dioxide gas disinfection spectrum against highly resistant hepatitis viruses [20-22]. Lu and team conducted a comparative disinfection efficacy of Chlorine Dioxide and hypochlorous acid in the soiled rooms and dishwashing areas of infectious disease wards and reported the superior activity of Chlorine Dioxide. Hence Taiwan Environmental Protection Bureau recommends twice-daily disinfection of hospital wards with Chlorine Dioxide to meet the indoor air quality guidelines [23]. Suen and team used Chlorine Dioxide as an antibacterial coating in filters of air purifiers, which significantly reduced the number of harmful microorganisms in the air [24]. Wang and team demonstrated the effectiveness ofChlorine Dioxidegas in effective removal of Organic Volatile Compounds (OVC) - benzene derivatives (gaseous benzene, toluene, o-xylene, and m-xylene) from water as well as from air without precipitating secondary pollution [25-27]. Hence apart from air fumigation for disinfection, Chlorine Dioxide gas is also used for Air pollution control [28].

Luftman and team efficiently used Chlorine Dioxide gas to successfully decontaminate a 4800 m3 facility with a total Chlorine Dioxide dosage of 400 ppm per hr in a single evening [29]. Liou and team investigated the sterilization effect of indoor air of laboratories, hospitals and conference rooms using Chlorine Dioxide gas - the disinfection efficacy of 90% was achieved in 30 minutes [30]. Lorcheim and team confirmed that Chlorine Dioxide gas can be used to disinfect beta-lactam manufacturing facility – a 3-log (99.9%) reduction of eight different beta-lactam suiteswas achieved successfully [31]. Lowe and team exposed Chlorine Dioxide gas at 10 different sites in a hospital and achieved germicidal efficacy of 7 to 10-log reductions of Acinetobacter baumannii, Escherichia coli, Enterococcus faecalis, Mycobacterium smegmatis, and Staphylococcus aureus [32]. Shirasaki and team applied Chlorine Dioxide gas as a sterilizer in a hospital (87 m3) for 3 h. Under 80% relative humidity, the colony of both Staphylococcus aureus and Escherichia coli was completely eradicated [33].

Chlorine Dioxide is an effective Sporicide and additionally used as an effective pesticide and insecticide to kill insects, pests, fleas, mites, bed bugs, mosquitoes, beetles, cockroaches, worms, moths, parasites, cysts etc without harming the humans and animals [34-65]. Chlorine Dioxide is widely used for sterilization of Medical devices and Organ implants [66-75]. During disinfection or water treatment process, Chlorine Dioxide doesn't corrode, or stain or damage the environment or surrounding or in the place of utility. Hence there is no need of covering the electrical and electronic components / instruments / gadgets etc during Chlorine Dioxide exposure and also there is no need for Post exposure, cleaning or swabbing or mopping the area.

In India, for treating drinking water Chlorine powder is mainly used. Maharashtra based SVS aqua tech offer 5 Kg Sodium Chlorite in bucket pack @ 4250 INR for treating 25 Lakh litres of Water [76]. Vizag Chemicals in partnership with UK based Tristel offers Chlorine Dioxide technology for treatment of drinking water [77]. Maharashtra based Hanna Instruments offers a range of instrumentation for measuring Chlorine Dioxide in air and water [78]. Gujarat based Kresko Chemicals offers Chlorine Dioxide generation kits asRAPI-G® Fumigation Sachet @ 200 INR / sachet; RAPI-G® Fumigation Gel @ 299 INR / piece; RAPI-G® Disinfectant Card @ 120 INR / piece for disinfection; Additionally, Chlorine Dioxide Sachet @ 225 INR / bagis available for treating water [79]. Maharashtra based Bhabha Atomic Research Centre (BARC) has developed CLEAN - **C**h**L**orine Dioxid**E** rele**A**si**N**g Polymer for treating drinking water of various volume and is easily scalable [80].Gujarat based Asha Technocrats and Maharashtra based Pure Water offers Chlorine Dioxide generators under the brand name “Lotus” and “PureOx” respectively for treating drinking water [81-82]..

Problem Statement, Objective & Scope for research

Based on the details mentioned in Introduction section, it’s evident on the utility and significance of Chlorine Dioxide for varied applications. The Objective of the present research is to design a cost-effective product to generate Chlorine Dioxide gas which is easy to handle or operate or use by a layman or common man without any aid of generating device or application device and ensuring the generated Chlorine Dioxide gas issafe for humans and animals and at the same time it iseffective and efficient for disinfection and water treatment applications.Based on the reviewed literature and available patent information there are very few or limited details on Chlorine Dioxide gas generation method, its testing procedure, packing / precautionary measures for varied application [83-86]. This research work will actively address this GAP and will demonstrate the practicality in formulation, evaluation, packing design and commercialization of Chlorine Dioxide product for disinfection and water treatment.

Experiments, Results & Discussion

Before proceeding for the formulation experiments, it was decided to develop a simple and sensitive analytical method to determine the Concentration (parts per million - ppm) of Chlorine Dioxide gas. This will help to decide, design and optimize the qualitative and quantitative composition of reactant mixture for Chlorine Dioxide gas generation. An Iodometric method was devised that relies upon Chlorine Dioxide oxidizing iodide ions to iodine, which is then titrated with Sodium Thiosulphate. The titre value obtained was then subjected to simple calculation and deduced the concentration of released Chlorine Dioxide gas. Chemicals, reagents and apparatus utilized for the study includes, Sodium Thiosulphate (Avantor Performance Materials), 0.025N Sodium Thiosulphate, 0.1N Sodium Thiosulphate, Chlorine –free water, Potassium Iodide (Avantor Performance Materials), Potassium Dichromate (Avantor Performance Materials), Soluble Starch (Natural Starch), 250mL Iodine Flask (Borosil), Suitable gas generation - absorption system, Burette 50 mL (Borosil), Cotton (Carolina),Connecting tubes (Borosil), Suction pump (Vijaya Scientific), Hot air oven (Lab India), Fume hood (Lab India) and Burette stand (Vijaya Scientific). A suitable gas generation and absorption system was employed to dissolve the liberated Chlorine Dioxide in water (chlorine-free). For this experiment, two 250mL Iodine flask(s) was taken. Cotton was plugged on top of each flask to stop gas leakage. The two flask(s) are then connected using a connecting tubes (Borosil) in such a way that one flask contains product to be tested added to Chlorine-free water. The other flask contains 100mL of Chlorine-free water with tube dipped inside water. A light to medium vaccum suction (Vijaya Scientific) was applied to this flask for 2 minutes until the solution becomes dark yellow colour. This yellow colored solution having dissolved Chlorine Dioxide gas is treated with 2g of Potassium Iodide and kept in a dark place for 5 minutes. Standardise this solution by titrating with standard Sodium Thiosulfate in the presence of Potassium Iodide, Citric Acid (Avantor Performance Materials), and Starch as indicator. Like-wise a blank determination was performed. The following representation (Figure.1) is the calculation to determine the Concentration of released Chlorine Dioxide gas.

$$\text{Chlorine Dioxide in ppm} = \frac{(A-B) \times N \times 13.490}{\text{Volume of sample (mL)}}$$

A: mL titre value of sample
B: mL titre value of blank
N: Normality of $Na_2S_2O_3$

To finalize the analytical method and its utility, the marketed products that claim to release Chlorine Dioxide gas were sourced and tested. [Nysa Virus Block Out Sterilization Card @ 190 INR per piece; Befinitive Virus Shut Out Card (Made in Japan) Virus Blocker Environment / Air Sterilization / Sanitization Card @ 349

INR per piece; RAPI-G® Disinfectant Card @ 120 INR per piece; RAPI-G® Fumigation Sachet @ 200 INR per sachet] The analysis results of the marketed products is presented in table.1 below,

Table 1: Concentration of Chlorine Dioxide gas released from Marketed products (Iodometric Titration Method)

Sample description	Concentration of Chlorine Dioxide gas released in ppm	Remarks
Nysa Virus Block Out Sterilization Card @ 190 INR per piece	250	Sample not dissolved completely, it leaves some residue material which is not soluble
Befinitive Virus Shut Out Card (Made in Japan) Virus Blocker Environment / Air Sterilization / Sanitization Card @ 349 INR per piece	379	Sample not dissolved completely, it leaves some residue material which is not soluble
RAPI-G® Disinfectant Card @ 120 INR per piece for fumigation and disinfection	510	Sample not dissolved completely, it leaves some residue material which is not soluble
RAPI-G® Fumigation Sachet @ 200 INR per sachet	2327	Packing has two compartments, each had a sample and to be added combinely for testing. Both the samples dissolved completely without residue

In this research, Chlorine Dioxide Sterilization / Disinfectant card will not be designed due to the product's direct contact with the end user all the time and there is a risk in regular and routine inhalation of Chlorine Dioxide gas which may affect one's respiratory system. Also the product feature and its utility are designed in such a way it's difficult for the end user to keep the product out of reach of children and companion animals. Hence, based on the literature review, it was decided to design a reactant mixture that will generate Chlorine Dioxide gas of about 2500 ppm effective enough to efficiently disinfect / fumigate / sterilize 250 square feet (sq.ft) of area. To achieve the targeted 2500 ppm concentration of Chlorine Dioxide gas generation, different permutation and combination of reactant mixture involving Sodium Chlorite (Zed-Chem Pvt Ltd) and Citric Acid was tried and evaluated. Finally the ratio of 9.02:0.98 / 20.8 g: 2.2 g of Sodium Chlorite and Citric Acid were finalized. Sodium Chlorite and Citric Acid was added to a plastic bowl having 20 mL water resulted in generating Chlorine Dioxide gas (ClO_2) and the reaction scheme (Figure.2) is as follows,

$$5NaClO_2 + 4C_6H_8O_7 \rightarrow 5ClO_2 + 5NaC_6H_5O_7 + 4H_2O$$

Sodium Chlorite + Citric Acid → Chlorine Dioxide + Sodium Citrate + Water

The main advantage in this method is the reactant mixture doesn't need any equipment or instrument or aid or fumigator to disperse or diffuse or spray or plume or shower or jet the generated Chlorine Dioxide gas.

The next step is to determine the disinfection efficiency of the Chlorine Dioxide gas released from the above finalized reactant mixture. Volumetric Air Sampling (VAS) method was utilized for the Microbial determination or Anti-microbial effectiveness of Chlorine Dioxide gas. Sterilized Preincubated Soyabean Casein Digest Agar (SCDA – Hi Media) plates were used for air sampling. This testing was done in process suites with 110, 205 and 270 square feet area. All the vents and doors of the suites were closed. Before exposing the suite with Chlorine Dioxide gas, air sampling was taken. Then in each suiteChlorine Dioxide gas was generated by adding 20.8 g of Sodium Chlorite, 2.2 g of Citric Acid into20 mL water.Post Chlorine Dioxide gas exposure, Volumetric Air Sampling was done in each suite at 30 min, 60 min & 90 min. All the sampled SCDA plates were incubated at 20-25°C for 3 days followed by 30-35°C for 2 days. After completion of incubation period, the plate colonies were counted using Colony counter and the results are tabulated in the following table 2.

From the below tabulated results, the disinfection efficiency of Chlorine Dioxide is evident. There is a 4-5 times reduction in microbial load in every suite within 30 minutes of Chlorine Dioxide exposure. In all the suites, disinfection was complete (microbe free) within 60 minutes of Chlorine Dioxide exposure.

Table 2: Microbiological air sampling results for areas exposed to Chlorine Dioxide gas

Testing Particulars	CFU/Plate in 110 Sq ft	CFU/Plate in 205 Sq ft	CFU/Plate in 270 Sq ft
Before Chlorine Dioxide exposure	118	122	115
30 min after Chlorine Dioxide exposure	25	31	22
60 min after Chlorine Dioxide exposure	0	1	0
90 min after Chlorine Dioxide exposure	0	0	0

During the performance of this study, occupational exposure of Chlorine Dioxide gas was inferred and found nauseating during Air Sampling at 30 minutes but felt manageable at 60 minutes and 90 minutes.

Further a microbial challenge study was performed to test the real-time disinfection effectiveness of Chlorine Dioxide gas. For this study, the American Type Culture Collection (ATCC) grade microorganisms were used viz. Escherichia coli (E.coli) – a gram-negative, facultative anaerobic, rod-shaped, coli form bacterium; Klebsiella pneumoniae – a gram-negative, non-motile, encapsulated anaerobic rod-shaped bacterium; Staphylococcus aureus (S.aureus) – a gram-positive, facultative anaerobic, spherically shaped bacterium; Clostridium sporogenes – a gram-positive, anaerobic, rod-shaped bacterium; Bacillus subtilis (B.subtilis) – a gram-positive, obligate aerobe, facultative anaerobic, rod-shaped bacterium; Aspergillus brasiliensis (A.brasiliensis) – a spore producing fungitolerant to temperature variances from extreme heat to freezing; Candida albicans (C.albicans) – an opportunistic yeast and a commensal organism. The mentioned microorganisms were grown in appropriate culture medium as per United States Pharmacopoeia (USP).Before exposing the room with Chlorine Dioxide gas, as done in the previous study a Volumetric Air Sampling (VAS) was done and CFU was determined using SCDA plates. Then all the vents and doors in the room were closed. The cultured plate of every organism – total 3 sets of each microorganism per room (21 no's in total) was kept scattered covering every nook and corner in 3 different rooms having 160, 250 and 330 square feet. Then in each room Chlorine Dioxide gas was generated by adding 20.8 g of Sodium Chlorite, 2.2 g of Citric Acid into 20 mL water. Post Chlorine Dioxide gas exposure, microbial culture plates was withdrawn from each room at 30 min, 60 min & 90 min i.e. 1 set of each microorganism'sculture plate (7 no's) per time point from every room was withdrawn. All the sampled or withdrawn culture plates containing microorganisms were incubated. After completion of incubation period, the colonies were counted and the results are tabulated in the following table 3.

Table 3: Microbiological challenge study & disinfection effectiveness of Chlorine Dioxide gas

Testing Particulars	CFU/Plate in 160 Sq ft			CFU/Plate in 250 Sq ft			CFU/Plate in 330 Sq ft		
Before Chlorine Dioxide Exposure	116			110			210		
Microbial Challenge Study	**Chlorine Dioxide Exposure**								
	30 min	60 min	90 min	30 min	60 min	90 min	30 min	60 min	90 min
Escherichia coli (E.coli)	10	0	0	9	0	0	12	0	0
Klebsiella pneumoniae	2	0	0	2	0	0	5	0	0
Staphylococcus aureus (S.aureus)	3	0	0	6	0	0	8	0	0
Clostridium sporogenes	8	0	0	8	0	0	11	0	0
Bacillus subtilis (B.subtilis)	1	0	0	6	0	0	4	0	0
Aspergillus brasiliensis (A.brasiliensis)	4	0	0	6	0	0	7	0	0
Candida albicans (C.albicans)	7	0	0	7	0	0	10	0	0

The above results are in-fact reinforcing the disinfection effectiveness of Chlorine Dioxide gas and the microbial challenge study results reciprocate and reproduce the findings observed in the microbial air sampling test results. The test findings is in-line with the literature evidence showing the achievability of microbe free environment using Chlorine Dioxide gas within short span of time.

After successful completion of formulation and evaluation, the next obvious step is to commercialize the product for public use. Before advancing, it was decided to evaluate and include proper stage gates in the commercial manufacturing process, mode of packing design & its requirements followed by stability evaluation of the product in intended packing configuration. The reactant mixture containing Sodium Chlorite and Citric Acid is hygroscopic and in presence of moisture or water they tend to react immediately and release Chlorine

Dioxide gas. Hence it was decided to design the manufacturing and packing process under de-humidified environment (25±5°C / 35±5%RH). Also the reactant mixture and the end product are light sensitive and undergo degradation – hence the manufacturing and packing to be performed under Sodium Vapor Lamp (SVP) lighting. On the packing aspect, a 3 ply heavy thickness pre-printed labeled aluminum sachet pouch having 3 sides sealed with 2 pockets / compartments inside – one for Sodium Chlorite and the other for Citric Acid with single induction seal liner and cut through provision at the top part or mouth portion was designed. The steps involved in the manufacturing & packing includes, weighing;Purging Nitrogen into aluminum sachet pouch before filling the reactant mixture; stand-alone parallel filling of Sodium Chlorite and Citric Acid individually into the compartments; nitrogen blanketing of the head space prior to induction sealing of aluminum sachet pouch. An outer preprinted carton (secondary packing) was designed to hold 25 no's of sachet pouch.

Two (2) such filled cartons were exposed to 40°C / 75%RH for 6 months. At the end of 6 months, the samples were sent to National Institute of Pharmaceutical Education & Research Centre (NIPER) for evaluation.Volumetric Air Sampling (VAS) method was utilized to investigate the disinfectant effectiveness of stability exposed samples. Sterilized Preincubated Soyabean Casein Digest Agar (SCDA – VWR) plates were used for air sampling. This testing was done in workplace with 105, 250 & 450 square feet area. All the vents and doors of the workplace were closed. Before exposing the workplace with Chlorine Dioxide gas, air sampling was taken. Then in each work place, Chlorine Dioxide gas was generated by emptying 1 sachet pouch into 20 mL water. Post Chlorine Dioxide gas exposure, Volumetric Air Sampling was done in each workplace at every 30 minutes time interval. All the sampled SCDA plates were incubated at 25°C for 3 days followed by 37°C for 3 days and then plate colonies were counted. Below are the results and images (Table 4-6)

Table 4: Stability evaluation of reactant mixturestored at40°C / 75%RH for 6 months and its effectiveness in generating Chlorine Dioxide to disinfect 105 Sq ft of work space

Testing Particulars	Bacterial colony Numbers (CFU)	Fungal Isolate Numbers	Others
Before Chlorine Dioxide Exposure	10	3	0
30 min after Chlorine Dioxide Exposure	1	0	0
60 min after Chlorine Dioxide Exposure	0	0	0
120 min after Chlorine Dioxide Exposure	0	0	0

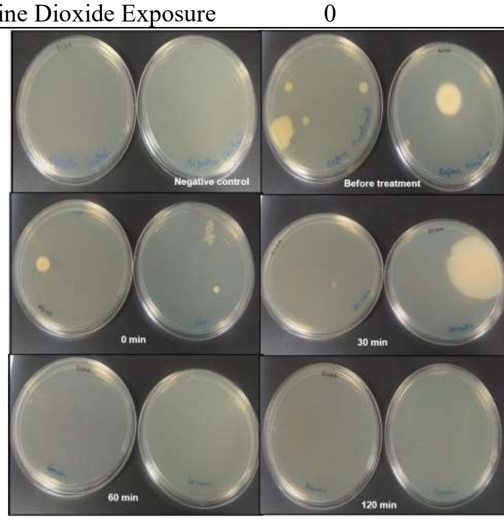


Table 5: Stability evaluation of reactant mixture stored at 40°C / 75%RH for 6 months and its effectiveness in generating Chlorine Dioxide to disinfect 250 Sq ft of work space

Testing Particulars	Bacterial colony Numbers (CFU)	Fungal Isolate Numbers	Others
Before Chlorine Dioxide Exposure	11	5	0
30 min after Chlorine Dioxide Exposure	3	1	0
60 min after Chlorine Dioxide Exposure	0	0	0
120 min after Chlorine Dioxide Exposure	0	0	0

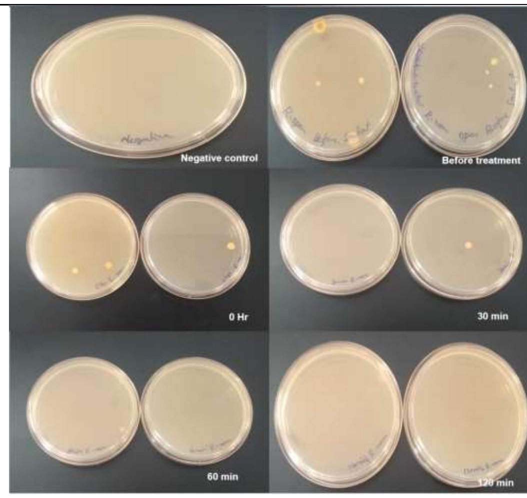
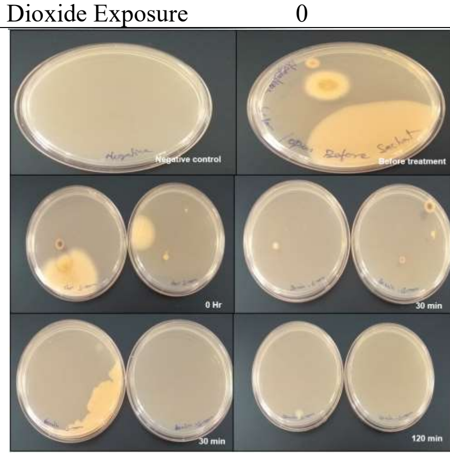


Table 6: Stability evaluation of reactant mixture stored at 40°C / 75%RH for 6 months and its effectiveness in generating Chlorine Dioxide to disinfect 450 Sq ft of workspace

Testing Particulars	Bacterial colony Numbers (CFU)	Fungal Isolate Numbers	Others
Before Chlorine Dioxide Exposure	11	6	0
30 min after Chlorine Dioxide Exposure	6	1	0
60 min after Chlorine Dioxide Exposure	2	1 (Mat)	0
120 min after Chlorine Dioxide Exposure	0	0	0



From the above presented results,the product stability at accelerated storage condition is well established. An interesting observation is inferred from the above study on the disinfection efficiency of Chlorine Dioxide. The Microbicidal and Sporicidal activity of Chlorine Dioxide gas from a single sachet pouch can be effectively used for disinfecting 250 sq ft of work space only. For disinfecting work spaces larger than 250 sq ft, proportionally the sachet pouch has to be used additionally.

This novel Chlorine Dioxide product for disinfection was successfully commercialized under the brand name CAIR®. From marketing and distribution perspective as well as from financial feasibility view point, the minimum order quantity within India has been set as 1 carton containing 25 sachet pouches priced at981 INR @ 39.24 INR per sachet pouch.

Before starting the formulation activity on Acidulated Chlorine Dioxide Effervescent Tablets the prerequisite design attributes was set especially on the quantity or concentration of Chlorine Dioxide required for water treatment and also the knowhow on the admissible level of Chlorine Dioxide containing water suitable for consumption by humans and animals. Based on World Health Organization guidelines and other relevant literature reference [87-89] it was decided to target 0.8 mg / L or 0.8 ppm of Chlorine Dioxide concentration for effective treatment of water free from pathogens, pathogenic spores, parasites and parasite cysts [90]. Preliminary experiments were conducted to arrive for concentration of Sodium Chlorite and Citric Acid and were finalized at

7.2 mg and 0.8 mg respectively which gave 0.8 mg / L or 0.8 ppm of Chlorine Dioxide in water. The finalized composition of Acidulated Chlorine Dioxide Effervescent Tablets is presented in the table.7 below,

Table 7: Composition of Acidulated Chlorine Dioxide Effervescent Tablets

Item No	Ingredients	Make	mg / tablet
1	Sodium Chlorite	Zed-Chem	7.2
2	Citric Acid Anhydrous	Avantor	18
3	Sodium Bicarbonate (Effersoda)	SPI Pharma	16
4	Mannitol (Pearlitol Flash)	Roquette	28.8
5	Silicon Dioxide (Syloid 244 FP)	Grace	4
6	Magnesium Stearate (Hyqual)	Avantor	1
	Total Tablet Weight		**75 mg**

In the above composition, 7.2 mg of Sodium Chlorite and 0.8 mg of Citric Acid are the reactant mixture to produce Chlorine Dioxide gas. 17.2 mg of Citric Acid and 16 mg of Sodium Bicarbonate are the reactant mixture for producing effervescence leading to disintegration of tablet. The uniqueness of Sodium Bicarbonate (EFFERSODA) is its particles are surfaced modified with Sodium Carbonate to act as a protecting layer thereby increasing resistance to humidity and prevents premature effervescence [91]. 28.8 mg of Mannitol is used as a diluent / filler. PEARLITOL FLASH - a co-processed excipient of Mannitol & Starch in 80:20 ratio balances the compressibility, disintegration, binding & flow of the blend [92]. To impart moisture protection; anti-tacking tendency; flow aid; preventing the reactant mixture(s)to react at solid state level;4 mg of mesoporous silica (SYLOID 244FP) was used [93]. For lubrication of the blend and forease of tabletting, a vegetable grade Magnesium Stearate (HYQUAL) was used at 1 mg level [94]. The composition was optimized qualitatively and quantitatively. Care was taken during the selection of ingredients so that tablet dissolves quickly leaving no residue or insoluble matter in water for treatment..The final blend for compression was characterized and is presented in the table.8 below,

Table 8: Blend Characterization

Particulars	Results
Description	No rat holing tendency. Blend exhibits good air permeability. White to off white fine free flowing powder
Odor	Faint Chlorine odor
Water by Kf	1.2%
Particle Size Distribution	NLT 80% pass through #30 mesh
Bulk density (g / mL)	0.55
Tapped density (g / mL)	0.69
Compressibility (%)	20
Hausner Ratio	1.25

From the above tabulated information, blend characteristics like description, odor and moisture content are conducive for the product performance. The final blend very well qualifies for a direct blending and compression process based on the particle size distribution, density, flow and compressibility index characteristics. From manufacturing to packing, the environment was maintained at 25±5°C / 35±5%RH and all the process was performed using Sodium Vapour Lamp (SVP). Item no. 2, 3, 4 and 5were sifted through #30 ASTM (American Society for Testing & Materials) mesh and blended in a GANSONS double cone blender at 15 rpm (revolutions per minute) for 10 min. Then the whole blended material was sifted through #30 ASTM mesh and blended again for 10 min then the whole blended material was divided into 2 equal parts. One (1) part of blend was loaded into blender. Item no. 1 was sifted through #30 ASTM mesh and added to the blender. Then remaining part of blend was added to blender and blended for 10 min. Then the whole blended material was sifted through #30 ASTM mesh and blended again in for 10 min. Finally Item no. 6 was sifted through #40 ASTM mesh and added to blender contents and blended for 5 min. The final blend was compressed into tablets in a CADMACH tablet press using PACIFIC6 mm Round Flat Faced Bevel Edged 'D' Type Punch Tooling with embossing JAL4AL (in circular orientation) on Upper Punch and 8 on Lower Punch. The following are the tablet characterization details realized during manufacturing,

Table 9: Tablet Characterization

Particulars	Results
Tablet Appearance	White colored round tablets with debossing JAL4AL on one side and 8 on the other side
Tabletting processability	The blend supports for tabletting @ 500 tablets per minute
Weight (mg)	72-77
Thickness (mm)	2.00-2.50
Hardness (kP)	1-4
Friability (%)	0.25
Static Disintegration Time (1 tablet in 100 mL Water)	< 1 minute
Disintegration Time (USP)	< 30 secs
Water activity (aW)	0.43
1 tablet in 1 litre of water (Iodometric Method)	0.81 ppm of Chlorine Dioxide

Based on the above tabulated results it's evident on the blend compressibility and tabletting feasibility. During tabletting, weight variation was observed less than 3% to the target weight showing adequate blend flow. With 6 mm dimension, was able to achieve hardness upto 4 kP and the friability value of 0.25% shows compressibility, binding and mechanical strength of the tablets. Disintegration time results by Static and USP method is very encouraging and satisfactory for the intended function of the tablets. The water activity data of the tablet shows on the control in the moisture content of tablets due to formulation and process design and hence with proper handling and storage there is very minimal or no possibility of microbial growth or contamination during storage and shelf-life. The manufactured Acidulated Chlorine Dioxide Effervescent Tablet was tested for Chlorine Dioxide release with addition of 1 tablet to 1 litre of water and tested by Iodometric method showing 0.8 ppm release of Chlorine Dioxide sufficient enough to kill the pathogens, pathogen spores, parasites, parasite cysts etc. The manufactured tablets were packed in cold formed pre-printed aluminum blister pack (primary pack) using ELMAC Blister packing machine. The environment was maintained at 25±5°C / 35±5%RH in packing suite. The tablet packed blister cards are further arranged in preprinted carton (secondary pack) in 100's (10 tablets X 10 blisters), 500's (25 tablets X 20 blisters) & 1000's (25 Tablets X 40 blisters). The packed samples were subjected to stability testing at 40°C / 75%RH for 6 months and the results are tabulated below in table10.

Table 10: Accelerated Stability Testing & Tablet Characterization

Particulars	Initial	40°C/75%RH – 6 Months
Tablet Appearance	White colored round tablets with debossing JAL4AL on one side and 8 on the other side	Complies to Initial description
AssaySodium Chlorite (%)	101.3	100.9
Assay Citric Acid (%)	100.4	100.1
Water by Kf	1.4	1.6
Weight (mg)	72-77	72-76
Thickness (mm)	2.00-2.50	2.05-2.49
Hardness (kP)	1-4	1.2-3.8
Static Disintegration Time	< 1 minute	50 secs
Disintegration Time (USP)	< 30 secs	25 secs
1 tablet in 1 litre of water(Iodometric Method)	0.81 ppm of Chlorine Dioxide	0.8 ppm of Chlorine Dioxide
Packing Integrity	No sign of blister pocket bulging due to premature gas release	No sign of blister pocket bulging due to gas release

Based on the above presented stability data, it is evident on the product stability at accelerated storage condition. The designed packing configuration for the manufactured tablets is working to its functional and storage characteristics. The product doesn't lose the potency and the concentration of Chlorine Dioxide gas release on storage was comparable to the initial or finished product testing. The anti-microbial, sporicidal, anti-parasite and cysticidal activity of one (1) Acidulated Chlorine Dioxide Effervescent Tablet can be effectively used for treating 1 litre of water. For treating large quantity of water, proportionally the number of tablets has to be increased. This novel Acidulated Chlorine Dioxide Effervescent Tablet for water treatment was successfully commercialized within India under the brand name JAL4AL®. 1 carton containing 100's count, 500's count and 1000's count are priced at 38 INR, 190 INR & 380 INR respectively.

CONCLUSION

In this research work, we have successfully formulated, evaluated, pack-designed and commercialized Chlorine Dioxide product for disinfection and water treatment. It's been a challenging experience and patience testing research work, in bringing out a competitive and at the same time a cost effective product of Chlorine Dioxide. Since Chlorine Dioxide being a gas, our prime motive was in efficient designing of suitable reactant mixture that will deliver the desired Chlorine Dioxide gas effective for the intended purpose of disinfection and water treatment which we have realized after laborious experiments. Through this research, we have fulfilled the identified GAP mentioned in the preliminary section of this research article i.e. there is a dearth need of a simple but an efficient alternative to the existing methods of disinfection and water treatment being practiced in the market. Especially in India, the utility of Chlorine Dioxide for disinfection or water treatment is not popular due to poor understanding and awareness of the public in general and less familiarity among the personnel working in safety, health & environment (SHE) division of government in particular. Through this research and its outcome evidenced herein, we strongly hope to witness the familiarity, adoptability and regular use of Chlorine Dioxide product(s) by people of India for safe disinfection and effective treatment of drinking water supplies at an affordable cost.

CONFLICT OF INTEREST

None

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