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Case Study

A Laboratory Accident of Acryloyl Chloride, Its Consequences, Treatment, and Safety Measures: An Arduous Lesson to All Researchers

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ABSTRACT: Research and teaching have an array of unique hazards that reflects both the variety and continuous evaluation of their operation. These include technical, physical, chemical, or biological hazards. We are reporting a laboratory accident involving acryloyl chloride (chemical hazard), its consequences, safety precautions, and the lesson learned from this incident. Acryloyl chloride is a highly toxic and volatile liquid. After being accidentally exposed to acryloyl chloride, a victim experienced blackout, headache, dizziness, tiredness, nose bleeding, persistent burning of the eyes, and intense nausea and vomiting. A victim reported two distinct hazardous effects, namely, nose bleeding and stomach ulcers, which were not mentioned in the SDS of acryloyl chloride. To avoid further exacerbation of consequences of acryloyl chloride accident, it may be preferable to initiate steroidal therapy along with symptomatic treatment from the start. The accidental consequences and lessons learned from this tragedy will serve as guiding factors for research scholars, postdoctoral fellows, principal investigators (PI), safety professionals, institutions, occupational health nurses, physicians, and toxicologists to prevent anything similar from happening again in the future.

KEYWORDS: *acryloyl chloride, eye burning, nausea and vomiting, ulcer, laboratory accident*

1. INTRODUCTION

As scientific discoveries in the field of chemistry advance, researchers should become more aware of the health risks associated with laboratory work.[1,2] Unfortunately, lab accident statistics show that laboratory accidents are entirely too common.[3−8] Contributing factors to the accident can be recognized at different levels: the institution, the department, the laboratory, the individual, and the discipline itself.[9−14] According to researchers in the field of occupational safety, accidents are most likely to occur when multiple individual and system failures coincide.[15]

Due to the propensity for victim-blaming, post-incident investigations are frequently perceived as being punishing rather than new learning opportunities. This leads to a poor accident investigation in which only the primary cause is identified rather than the underlying causes.[16] As a result, negative attitudes toward safety policies and procedures are becoming more prevalent, poisoning the attitudes of future generations of students, and increasing the rate of under-reporting.[7] Institutions and PIs have an ethical obligation to provide comprehensive safety training on the use of reagents and chemicals.[17]

Several high-profile accidents in academic laboratories around the world have occurred in the last ten years, resulting in serious injuries and fatalities. Following these incidents, calls for reflection and re-examination of the academic discipline's approach to safety research and policy are common. However, the study of academic lab safety is still primitive, and data on changes in safety attitudes and behaviors is desperately needed.[7] With this context in mind, here we are reporting a laboratory accident of acryloyl chloride, its consequences, treatments, and safety measures. To the best of our knowledge, this is the third report on the acryloyl chloride accident.[18,19] Acryloyl chloride is a pale yellow, highly toxic, volatile liquid that is used in the synthesis of irreversible inhibitors and biomaterials.[20] It can cause eye and mucosal surface irritation, pneumonia, pulmonary edema, and even death.[20] According to the previous two reports, victims suffered from non-cardiogenic pulmonary edema, mild sore throat, eye discomfort, and acute respiratory distress syndrome (ARDS).[18,19] In our case, we noticed eye discomfort, nausea and vomiting, nose bleeding, and stomach ulceration. Nose bleeding and stomach ulcers were two distinct hazardous

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SAFETY DATA SHEET

Acryloyl chloride **Revision Date** 14-Feb-2020

Revision Date 14-Feb-2020 **Revision Number** 3

2. Hazard(s) identification

Classification

This chemical is considered hazardous by the 2012 OSHA Hazard Communication Standard (29 CFR 1910.1200)

Flammable liquids	Category 2
Acute oral toxicity	Category 4
Acute Inhalation Toxicity - Vapors	Category 1
Skin Corrosion/Irritation	Category 1 B
Serious Eye Damage/Eye Irritation	Category 1
Specific target organ toxicity (single exposure)	Category 3
Target Organs - Respiratory system.	

Label Elements

Signal Word

Danger

Hazard Statements

Highly flammable liquid and vapor
Harmful if swallowed

Causes severe skin burns and eye damage
May cause respiratory irritation
Fatal if inhaled

Precautionary Statements

Prevention

Wash face, hands and any exposed skin thoroughly after handling
Do not eat, drink or smoke when using this product
Do not breathe dust/fume/gas/mist/vapors/spray
Use only outdoors or in a well-ventilated area
Wear respiratory protection
Wear protective gloves/protective clothing/eye protection/face protection
Keep away from heat/sparks/open flames/hot surfaces. - No smoking
Keep container tightly closed
Ground/bond container and receiving equipment
Use explosion-proof electrical/ventilating/lighting/equipment
Use only non-sparking tools
Take precautionary measures against static discharge
Keep cool

Response

Immediately call a POISON CENTER or doctor/physician

Inhalation

IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing

Skin

IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse

Eyes

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing

Ingestion

Rinse mouth
Do NOT induce vomiting

Fire

In case of fire: Use CO2, dry chemical, or foam for extinction

Storage

Store in a well-ventilated place. Keep container tightly closed
Store locked up

Disposal

Dispose of contents/container to an approved waste disposal plant

Hazards not otherwise classified (HNOC)

Reacts violently with water

Figure 1a. Hazard statement from the SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

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Fatal if inhaled

Precautionary Statements
Prevention
Wash face, hands and any exposed skin thoroughly after handling
Do not eat, drink or smoke when using this product
Do not breathe dust/fume/gas/mist/vapors/spray
Use only outdoors or in a well-ventilated area
Wear respiratory protection
Wear protective gloves/protective clothing/eye protection/face protection
Keep away from heat/sparks/open flames/hot surfaces. - No smoking
Keep container tightly closed
Ground/bond container and receiving equipment
Use explosion-proof electrical/ventilating/lighting/equipment
Use only non-sparking tools
Take precautionary measures against static discharge
Keep cool
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Immediately call a POISON CENTER or doctor/physician
Inhalation
IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing
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IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/shower
Wash contaminated clothing before reuse
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IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
Ingestion
Rinse mouth
Do NOT induce vomiting
Fire
In case of fire: Use CO2, dry chemical, or foam for extinction
Storage
Store in a well-ventilated place. Keep container tightly closed
Store locked up
Disposal
Dispose of contents/container to an approved waste disposal plant
Hazards not otherwise classified (HNOC)
Reacts violently with water

3. Composition/Information on Ingredients

Component	CAS-No	Weight %
Acryloyl chloride	814-68-6	<= 100
Phenothiazine	92-84-2	<= 0.1

4. First-aid measures

Page 2 / 8

Figure 1b. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

General Advice	Show this safety data sheet to the doctor in attendance. Immediate medical attention is required.
Eye Contact	Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. In the case of contact with eyes, rinse immediately with plenty of water and seek medical advice.
Skin Contact	Wash off immediately with plenty of water for at least 15 minutes. Immediate medical attention is required.
Inhalation	If not breathing, give artificial respiration. Do not use mouth-to-mouth method if victim ingested or inhaled the substance; give artificial respiration with the aid of a pocket mask equipped with a one-way valve or other proper respiratory medical device. Remove to fresh air. Immediate medical attention is required.
Ingestion	Do NOT induce vomiting. Call a physician or poison control center immediately.
Most important symptoms and effects	Causes burns by all exposure routes. Difficulty in breathing. Inhalation of high vapor concentrations may cause symptoms like headache, dizziness, tiredness, nausea and vomiting: Product is a corrosive material. Use of gastric lavage or emesis is contraindicated. Possible perforation of stomach or esophagus should be investigated: Ingestion causes severe swelling, severe damage to the delicate tissue and danger of perforation
Notes to Physician	Treat symptomatically

5. Fire-fighting measures

Suitable Extinguishing Media	CO_2, dry chemical, dry sand, alcohol-resistant foam. Water mist may be used to cool closed containers.
Unsuitable Extinguishing Media	No information available
Flash Point	-4 °C / 24.8 °F
Method -	No information available
Autoignition Temperature	No information available
Explosion Limits	
Upper	No data available
Lower	No data available
Sensitivity to Mechanical Impact	No information available
Sensitivity to Static Discharge	No information available

Specific Hazards Arising from the Chemical
Thermal decomposition can lead to release of irritating gases and vapors. The product causes burns of eyes, skin and mucous membranes. Reacts violently with water. Flammable. Containers may explode when heated. Vapors may form explosive mixtures with air. Vapors may travel to source of ignition and flash back.

Hazardous Combustion Products
Carbon monoxide (CO). Carbon dioxide (CO_2). Hydrogen chloride.
Protective Equipment and Precautions for Firefighters
As in any fire, wear self-contained breathing apparatus pressure-demand, MSHA/NIOSH (approved or equivalent) and full protective gear. Thermal decomposition can lead to release of irritating gases and vapors.

NFPA

Health	Flammability	Instability	Physical hazards
4	3	2	W

Page 3 / 8

Figure 1c. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

6. Accidental release measures

Personal Precautions Ensure adequate ventilation. Use personal protective equipment as required. Evacuate personnel to safe areas. Keep people away from and upwind of spill/leak. Remove all sources of ignition. Take precautionary measures against static discharges.

Environmental Precautions Should not be released into the environment. See Section 12 for additional Ecological Information.

Methods for Containment and Clean Up Soak up with inert absorbent material. Keep in suitable, closed containers for disposal. Do not expose spill to water. Remove all sources of ignition. Use spark-proof tools and explosion-proof equipment.

7. Handling and storage

Handling Wear personal protective equipment/face protection. Do not get in eyes, on skin, or on clothing. Use only under a chemical fume hood. Do not breathe mist/vapors/spray. Do not ingest. If swallowed then seek immediate medical assistance. Do not allow contact with water. Handle under an inert atmosphere. Keep away from open flames, hot surfaces and sources of ignition. Use only non-sparking tools. To avoid ignition of vapors by static electricity discharge, all metal parts of the equipment must be grounded. Take precautionary measures against static discharges.

Storage Corrosives area. Keep away from heat, sparks and flame. Store under an inert atmosphere. Protect from moisture. Keep containers tightly closed in a dry, cool and well-ventilated place. Keep away from water or moist air.

8. Exposure controls / personal protection

Exposure Guidelines

Component	ACGIH TLV	OSHA PEL	NIOSH IDLH	Mexico OEL (TWA)
Phenothiazine	TWA: 5 mg/m³ Skin	(Vacated) TWA: 5 mg/m³ Skin	TWA: 5 mg/m³	TWA: 5 mg/m³

Legend

ACGIH - American Conference of Governmental Industrial Hygienists
OSHA - Occupational Safety and Health Administration
NIOSH IDLH: NIOSH - National Institute for Occupational Safety and Health

Engineering Measures Ensure that eyewash stations and safety showers are close to the workstation location. Ensure adequate ventilation, especially in confined areas. Use explosion-proof electrical/ventilating/lighting/equipment.

Personal Protective Equipment

Eye/face Protection Wear appropriate protective eyeglasses or chemical safety goggles as described by OSHA's eye and face protection regulations in 29 CFR 1910.133 or European Standard EN166.

Skin and body protection Wear appropriate protective gloves and clothing to prevent skin exposure.

Respiratory Protection Follow the OSHA respirator regulations found in 29 CFR 1910.134 or European Standard EN 149. Use a NIOSH/MSHA or European Standard EN 149 approved respirator if exposure limits are exceeded or if irritation or other symptoms are experienced.

Hygiene Measures Handle in accordance with good industrial hygiene and safety practice.

9. Physical and chemical properties

Physical State Liquid

Page 4 / 8

Figure 1d. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

Appearance	Clear
Odor	Acrid
Odor Threshold	No information available
pH	Not applicable
Melting Point/Range	No data available
Boiling Point/Range	74 - 76 °C / 165.2 - 168.8 °F
Flash Point	-4 °C / 24.8 °F
Evaporation Rate	No information available
Flammability (solid,gas)	Not applicable
Flammability or explosive limits	
Upper	No data available
Lower	No data available
Vapor Pressure	No information available
Vapor Density	3.12
Specific Gravity	1.114
Solubility	Reacts violently with water
Partition coefficient; n-octanol/water	No data available
Autoignition Temperature	No information available
Decomposition Temperature	No information available
Viscosity	No information available
Molecular Formula	C3H3ClO
Molecular Weight	90.51

10. Stability and reactivity

Reactive Hazard	Yes
Stability	Stable under recommended storage conditions. UNSTABLE (REACTIVE) UPON DEPLETION OF INHIBITOR.
Conditions to Avoid	Keep away from open flames, hot surfaces and sources of ignition. Exposure to moist air or water. Exposure to light. Heat. Exposure to moisture.
Incompatible Materials	Bases, Water, Amines, Oxidizing agent
Hazardous Decomposition Products	Carbon monoxide (CO), Carbon dioxide (CO_2), Hydrogen chloride
Hazardous Polymerization	Hazardous polymerization does not occur.
Hazardous Reactions	None under normal processing. Reacts violently with water.

11. Toxicological information

Acute Toxicity

Product Information
Component Information

Component	LD50 Oral	LD50 Dermal	LC50 Inhalation
Phenothiazine	LD50 = 5000 mg/kg (Rat)	>2000 mg/kg (Rabbit)	>5 mg/L/4h (Rat)

Toxicologically Synergistic Products No information available

Delayed and immediate effects as well as chronic effects from short and long-term exposure

Irritation No information available

Sensitization No information available

Carcinogenicity The table below indicates whether each agency has listed any ingredient as a carcinogen.

Component	CAS-No	IARC	NTP	ACGIH	OSHA	Mexico

Page 5 / 8

Figure 1e. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

Acryloyl chloride	814-68-6	Not listed	Not listed	Not listed	Not listed	Not listed
Phenothiazine	92-84-2	Not listed	Not listed	Not listed	Not listed	Not listed

Mutagenic Effects No information available

Reproductive Effects No information available.

Developmental Effects No information available.

Teratogenicity No information available.

STOT - single exposure Respiratory system
STOT - repeated exposure None known

Aspiration hazard No information available

Symptoms / effects,both acute and delayed Inhalation of high vapor concentrations may cause symptoms like headache, dizziness, tiredness, nausea and vomiting: Product is a corrosive material. Use of gastric lavage or emesis is contraindicated. Possible perforation of stomach or esophagus should be investigated: Ingestion causes severe swelling, severe damage to the delicate tissue and danger of perforation

Endocrine Disruptor Information No information available

Other Adverse Effects The toxicological properties have not been fully investigated.

12. Ecological information

Ecotoxicity

Reacts with water so no ecotoxicity data for the substance is available.

Component	Freshwater Algae	Freshwater Fish	Microtox	Water Flea
Phenothiazine	Not listed	LC50: = 1.1 mg/L, 48h (Oryzias latipes) LC50: = 0.579 mg/L, 96h (Oncorhynchus mykiss)	Not listed	EC50: 0.154 mg/L, 48h (Daphnia)

Persistence and Degradability Persistence is unlikely based on information available.

Bioaccumulation/ Accumulation No information available.

Mobility Will likely be mobile in the environment due to its volatility.

Component	log Pow
Phenothiazine	4.24

13. Disposal considerations

Waste Disposal Methods Chemical waste generators must determine whether a discarded chemical is classified as a hazardous waste. Chemical waste generators must also consult local, regional, and national hazardous waste regulations to ensure complete and accurate classification.

14. Transport information

DOT
UN-No UN3383
Proper Shipping Name TOXIC BY INHALATION LIQUID, FLAMMABLE, N.O.S.
Technical Name Phenothiazine
Hazard Class 6.1
Subsidiary Hazard Class 3
Packing Group I
TDG Forbidden
IATA FORBIDDEN FOR IATA TRANSPORT
UN-No UN3383

Page 6 / 8

Figure 1f. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

Proper Shipping Name	TOXIC BY INHALATION LIQUID, FLAMMABLE, N.O.S.*
Hazard Class	6.1
Subsidiary Hazard Class	3

IMDG/IMO

UN-No	UN3383
Proper Shipping Name	TOXIC BY INHALATION LIQUID, FLAMMABLE, N.O.S.
Hazard Class	6.1
Subsidiary Hazard Class	3
Packing Group	I

15. Regulatory information

United States of America Inventory

Component	CAS-No	TSCA	TSCA Inventory notification - Active/Inactive	TSCA - EPA Regulatory Flags
Acryloyl chloride	814-68-6	X	ACTIVE	-
Phenothiazine	92-84-2	X	ACTIVE	-

Legend:
TSCA - Toxic Substances Control Act, (40 CFR Part 710)
X - Listed
'-' - Not Listed

TSCA 12(b) - Notices of Export Not applicable

International Inventories
Canada (DSL/NDSL), Europe (EINECS/ELINCS/NLP), Philippines (PICCS), Japan (ENCS), Australia (AICS), China (IECSC), Korea (ECL).

Component	CAS-No	DSL	NDSL	EINECS	PICCS	ENCS	AICS	IECSC	KECL
Acryloyl chloride	814-68-6	-	X	212-399-0	X	X	X	X	KE-29735
Phenothiazine	92-84-2	X	-	202-196-5	X	X	X	X	KE-28250

U.S. Federal Regulations

SARA 313 Not applicable

SARA 311/312 Hazard Categories See section 2 for more information

CWA (Clean Water Act) Not applicable

Clean Air Act Not applicable

OSHA - Occupational Safety and Health Administration Not applicable

Component	Specifically Regulated Chemicals	Highly Hazardous Chemicals
Acryloyl chloride	-	TQ: 250 lb

CERCLA Not applicable

Component	Hazardous Substances RQs	CERCLA EHS RQs
Acryloyl chloride	-	100 lb

California Proposition 65 This product does not contain any Proposition 65 chemicals.

U.S. State Right-to-Know Regulations

Component	Massachusetts	New Jersey	Pennsylvania	Illinois	Rhode Island
Acryloyl chloride	X	X	X	-	-
Phenothiazine	X	X	X	-	X

Page 7 / 8

Figure 1g. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Acryloyl chloride **Revision Date** 14-Feb-2020

U.S. Department of Transportation
Reportable Quantity (RQ): N
DOT Marine Pollutant N
DOT Severe Marine Pollutant N

U.S. Department of Homeland Security This product contains the following DHS chemicals:
Legend - STQs = Screening Threshold Quantities, APA = A placarded amount

Component	DHS Chemical Facility Anti-Terrorism Standard
Acryloyl chloride	Release STQs - 10000lb

Other International Regulations

Mexico - Grade No information available

16. Other information

Prepared By Health, Safety and Environmental Department
Email: tech@alfa.com
www.alfa.com

Revision Date 14-Feb-2020
Print Date 14-Feb-2020
Revision Summary SDS authoring systems update, replaces ChemGes SDS No. 814-68-6/1.

Disclaimer
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text

End of SDS

Figure 1h. SDS of acryloyl chloride. Used with permission from ref 20. Copyright 2020 Thermo Fisher.

effects reported by the victim, which were not mentioned in the SDS of acryloyl chloride (Figures 1a−1h).

2. ACRYLOYL CHLORIDE ACCIDENT

2.1. Chemical Detail. Acryloyl chloride, also known as 2-propenoyl chloride or acrylic acid chloride, is an organic compound with the molecular formula of C_3H_3ClO. It has a CAS number of 814-68-6 and a PubChem CID of 13140. It was delivered in a glass bottle tightly packed with a rubber cork (Figure 2a), with a boiling point of 74−76 °C, a flash point of −4 °C, and a vapor pressure of 106.6 hPa (20 °C).[20] PubChem Laboratory Chemical Safety Summaries (LCSSs) for acryloyl chloride are available at https://pubchem.ncbi.nlm.nih.gov/compound/Acryloyl-chloride#section=Safety-and-Hazards&fullscreen=true.

2.2. Chemistry. Our cancer research laboratory is actively involved in the synthesis of irreversible EGFR tyrosine kinase inhibitors (EGFR TKI) and their testing against non-small cell lung cancer (NSCLC).[21,22] The most common reaction that is involved in the synthesis of irreversible EGFR TKI is the addition of the acryloyl group to the amino group of the intermediate (**1**) using acryloyl chloride (**2**) (Scheme 1).

A laboratory accident of acryloyl chloride occurred while synthesizing the irreversible EGFR TKI as given in Scheme 1.

2.3. Accident Detail. In August 2021, a Postgraduate (PG) student (accident victim) joined my lab to work on the NSCLC

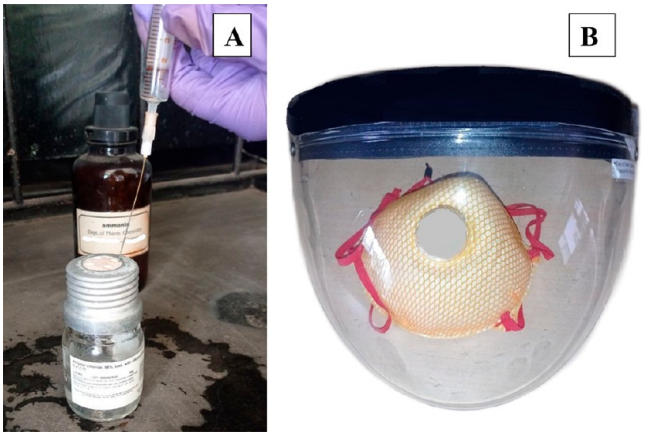

Figure 2. (a) Taking out acryloyl chloride in the fume hood using a glass syringe (ammonia sprinkled around the bottle of acryloyl chloride). (b) Helmet and N-90 mask used during the reaction.

project. Under my supervision, my two Ph.D. students and PG student (accident victim) set up the acrylation reaction as described in Scheme 1 on February 15, 2022. We (myself and my two Ph.D. students) were well-versed and trained in this reaction because we used to set it up with extreme caution on a regular basis. We were taking all the precautions outlined on the Safety Data Sheet (SDS) for acryloyl chloride (Figures

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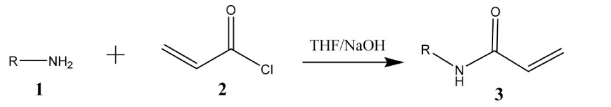
ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

Scheme 1. General Scheme of the Synthesis of Irreversible EGFR TKIs

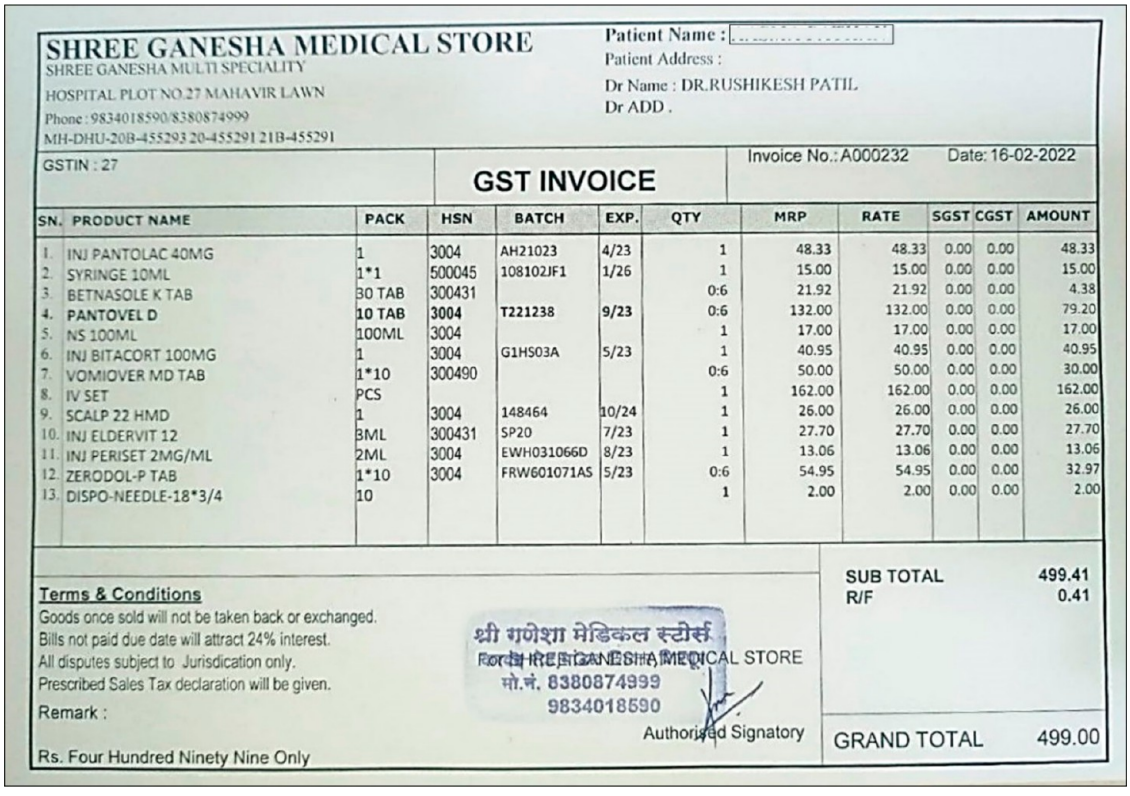


1a−1h).[20] According to risk assessment analysis, if acryloyl chloride was accidentally exposed, there would be a risk of eye irritation, weakness, skin sensitization, and breathing problems. As a result, we performed this reaction in a fume hood with a movable "shower with eyerinser" nearby. According to protocol, wearing personal protective equipment (PPE) is mandatory in the lab. I had already instructed a PG student to wear PPE, which included an N-90 mask, helmet, gloves, and an apron that covered the entire body (Figure 2). We took the bottle of acryloyl chloride directly from cool storage into the fume hood (acryloyl chloride is volatile and spreads quickly in the environment) and measured 2 mL (96%) with a glass syringe while wearing gloves, a helmet, and an N-90 mask. We sprinkled ammonia around the acryloyl chloride bottle before injecting the syringe into it to neutralize the fumes (Figure 2a). We stirred the reaction overnight at 0 °C in an iodine flask, and the next morning (February 16, 2022), we neutralized the excess acryloyl chloride by adding NaOH solution. The final stage was the evaporation of the content, which I thought could be handled by a PG student (accident victim). I instructed her to wear the helmet and N-90 mask while heating the flask in the fume hood and keep a safe distance from the beaker, and I went to attend the UG class. When I returned from class, a PG student (accident victim) came into my office, saying that the contents of the beaker had been bumped, and she was not feeling well, experiencing burning sensations in her eyes and blackouts.

"Did you wear a helmet and mask properly?" I inquired. Yes, she said. I calmed her down, rinsed her eyes with the eye washer, and then advised her to change clothes and take a shower. At first glance, I assumed she was in a panic state, that a small amount of acryloyl chloride fumes might have affected her, and the situation could be resolved as the helmet and mask would have protected her. However, that was not the case; she hid reality. Later, CC TV footage revealed that she was working there without a helmet and only with a mask (which was also not properly worn), and the fume hood door was partially closed during heating.

3. POST-ACCIDENT ANALYSIS (POST-ACCIDENT INCIDENCES, DIAGNOSIS, AND TREATMENT)

We exited the chemistry building and proceeded to the Ganesha hospital, which was within walking distance from campus. When we arrived at the hospital, she was having nausea and vomiting, as well as weakness and body aches. We discussed everything with the doctor and showed him the acryloyl chloride SDS. The doctor examined all the primary parameters of the PG student (accident victim), including blood pressure and a physical examination of the tongue and eyes. Except for the redness in the eyes, the physical examination revealed nothing abnormal. He began treating her symptomatically as recommended in the acryloyl chloride SDS (Figure 1c, *Notes to Physician*) and, via IV, administered a pantoprazole injection (to control acidity), betacort injection [corticosteroid (antiallergic)], Eldervit-12 injection [ascorbic acid, folic acid, niacinamide, and vitamin B12 (nutritional supplement to overcome weakness)], and Periset



SHREE GANESHA MEDICAL STORE
SHREE GANESHA MULTI SPECIALITY
HOSPITAL PLOT NO.27 MAHAVIR LAWN
Phone : 9834018590/8380874999
MH-DHU-20B-455293 20-455291 21B-455291

Patient Name :
Patient Address :
Dr Name : DR.RUSHIKESH PATIL
Dr ADD .

GSTIN : 27

GST INVOICE

Invoice No.: A000232 Date: 16-02-2022

SN.	PRODUCT NAME	PACK	HSN	BATCH	EXP.	QTY	MRP	RATE	SGST	CGST	AMOUNT
1.	INJ PANTOLAC 40MG	1	3004	AH21023	4/23	1	48.33	48.33	0.00	0.00	48.33
2.	SYRINGE 10ML	1*1	500045	108102JF1	1/26	1	15.00	15.00	0.00	0.00	15.00
3.	BETNASOLE K TAB	30 TAB	300431			0:6	21.92	21.92	0.00	0.00	4.38
4.	PANTOVEL D	10 TAB	3004	T221238	9/23	0:6	132.00	132.00	0.00	0.00	79.20
5.	NS 100ML	100ML	3004			1	17.00	17.00	0.00	0.00	17.00
6.	INJ BITACORT 100MG	1	3004	G1HS03A	5/23	1	40.95	40.95	0.00	0.00	40.95
7.	VOMIOVER MD TAB	1*10	300490			0:6	50.00	50.00	0.00	0.00	30.00
8.	IV SET	PCS				1	162.00	162.00	0.00	0.00	162.00
9.	SCALP 22 HMD	1	3004	148464	10/24	1	26.00	26.00	0.00	0.00	26.00
10.	INJ ELDERVIT 12	3ML	300431	SP20	7/23	1	27.70	27.70	0.00	0.00	27.70
11.	INJ PERISET 2MG/ML	2ML	3004	EWH031066D	8/23	1	13.06	13.06	0.00	0.00	13.06
12.	ZERODOL-P TAB	1*10	3004	FRW601071AS	5/23	0:6	54.95	54.95	0.00	0.00	32.97
13.	DISPO-NEEDLE-18*3/4	10				1	2.00	2.00	0.00	0.00	2.00

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Figure 3. Prescription of Ganesha hospital for a PG student (accident victim).

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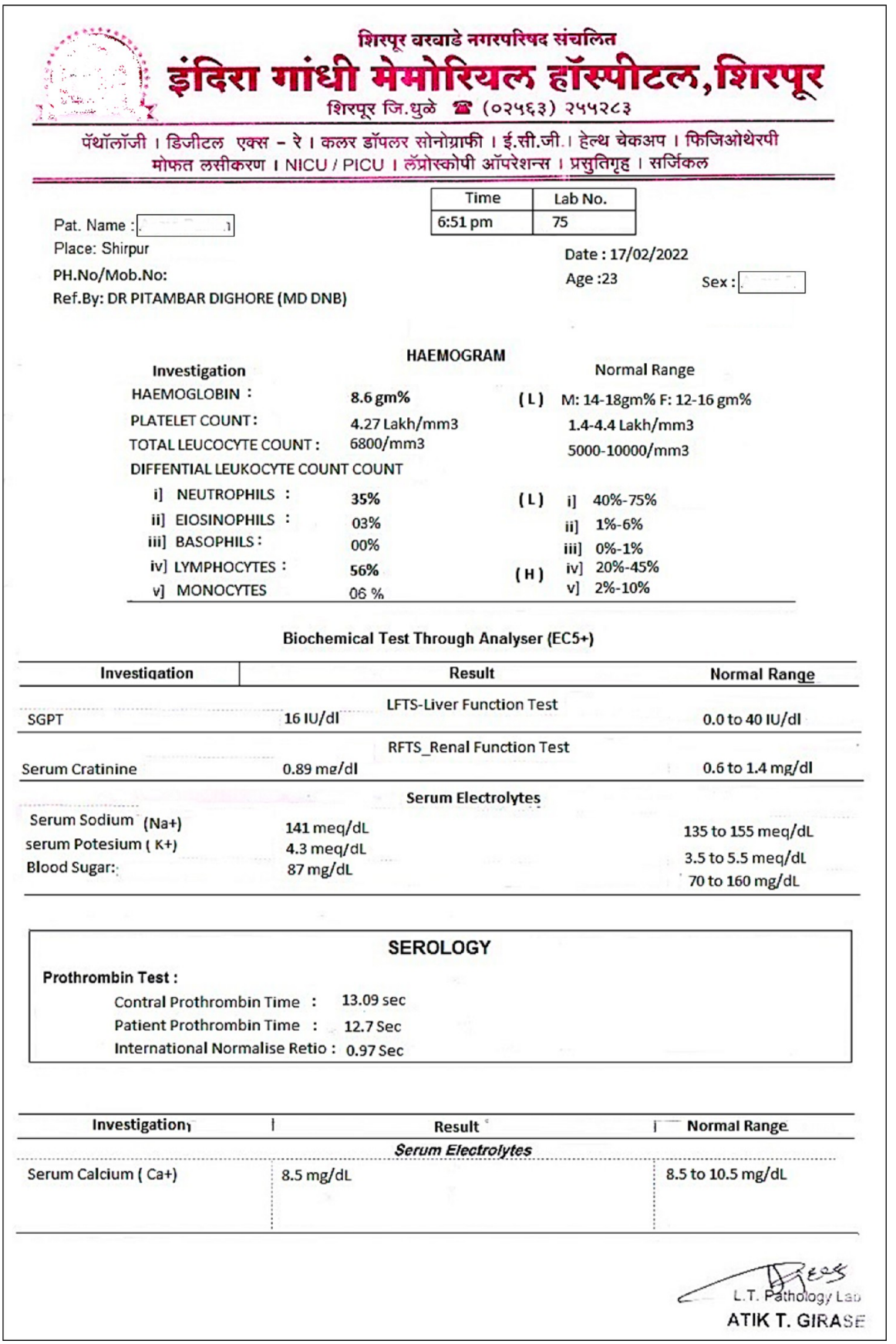

शिरपूर वरवाडे नगरपरिषद संचलित

इंदिरा गांधी मेमोरियल हॉस्पीटल, शिरपूर

शिरपूर जि.धुळे ☎ (०२५६३) २५५२८३

पॅथॉलॉजी । डिजीटल एक्स - रे । कलर डॉपलर सोनोग्राफी । ई.सी.जी. । हेल्थ चेकअप । फिजिओथेरपी
मोफत लसीकरण । NICU / PICU । लॅप्रोस्कोपी ऑपरेशन्स । प्रसुतिगृह । सर्जिकल

Time	Lab No.
6:51 pm	75

Pat. Name :
Place: Shirpur
PH.No/Mob.No:
Ref.By: DR PITAMBAR DIGHORE (MD DNB)

Date : 17/02/2022
Age :23 Sex :

HAEMOGRAM

Investigation			Normal Range
HAEMOGLOBIN :	8.6 gm%	(L)	M: 14-18gm% F: 12-16 gm%
PLATELET COUNT:	4.27 Lakh/mm3		1.4-4.4 Lakh/mm3
TOTAL LEUCOCYTE COUNT :	6800/mm3		5000-10000/mm3
DIFFENTIAL LEUKOCYTE COUNT COUNT			
i] NEUTROPHILS :	35%	(L)	i] 40%-75%
ii] EIOSINOPHILS :	03%		ii] 1%-6%
iii] BASOPHILS :	00%		iii] 0%-1%
iv] LYMPHOCYTES :	56%	(H)	iv] 20%-45%
v] MONOCYTES	06 %		v] 2%-10%

Biochemical Test Through Analyser (EC5+)

Investigation	Result	Normal Range
	LFTS-Liver Function Test	
SGPT	16 IU/dl	0.0 to 40 IU/dl
	RFTS_Renal Function Test	
Serum Cratinine	0.89 mg/dl	0.6 to 1.4 mg/dl
	Serum Electrolytes	
Serum Sodium (Na+)	141 meq/dL	135 to 155 meq/dL
serum Potesium (K+)	4.3 meq/dL	3.5 to 5.5 meq/dL
Blood Sugar:	87 mg/dL	70 to 160 mg/dL

SEROLOGY

Prothrombin Test :

Contral Prothrombin Time :	13.09 sec
Patient Prothrombin Time :	12.7 Sec
International Normalise Retio :	0.97 Sec

Investigation	Result	Normal Range
	Serum Electrolytes	
Serum Calcium (Ca+)	8.5 mg/dL	8.5 to 10.5 mg/dL

L.T. Pathology Lab
ATIK T. GIRASE

Figure 4. Biochemical testing reports of a PG student (accident victim).

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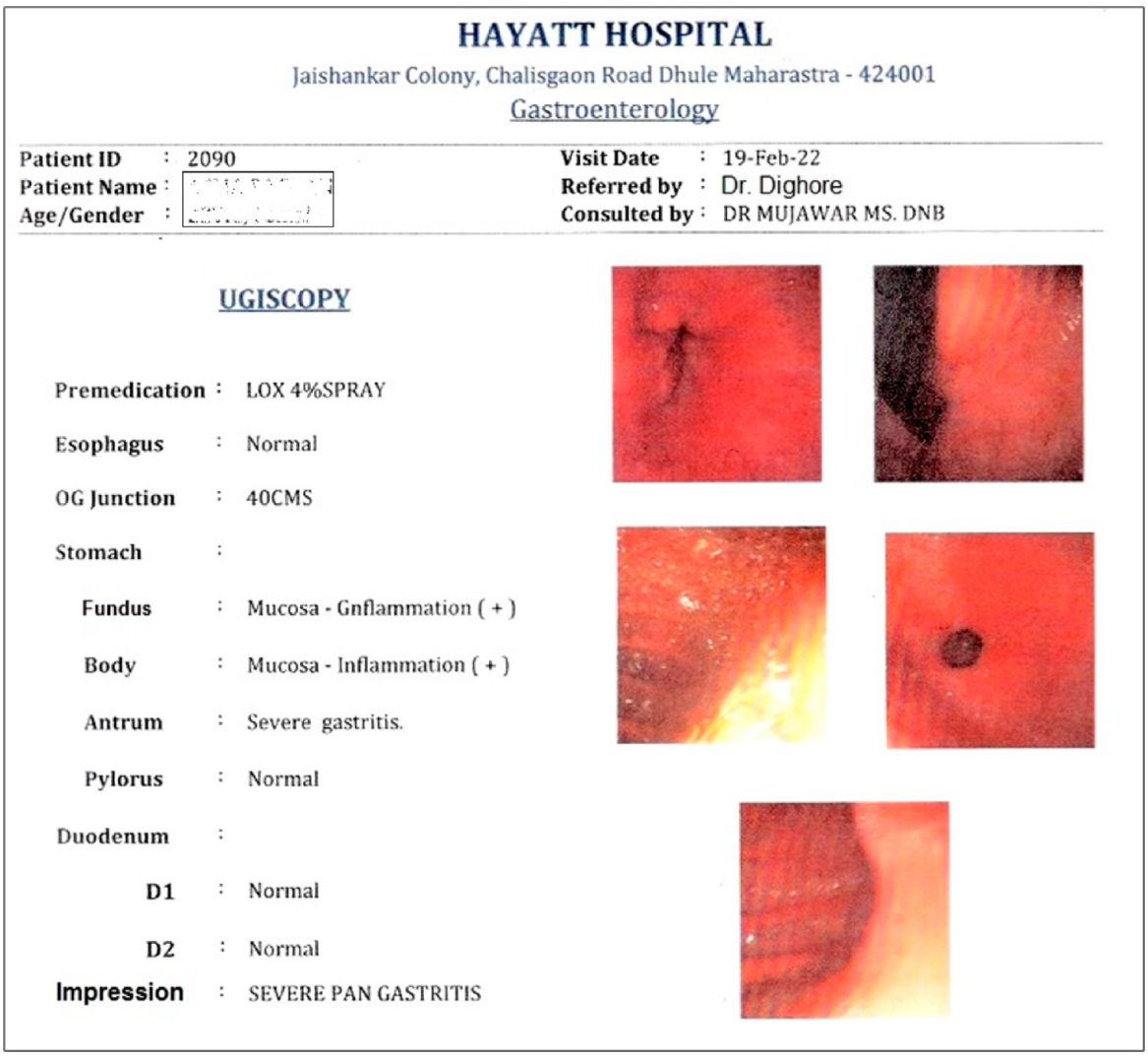
HAYATT HOSPITAL

Jaishankar Colony, Chalisgaon Road Dhule Maharastra - 424001

Gastroenterology

Patient ID : 2090
Patient Name :
Age/Gender :

Visit Date : 19-Feb-22
Referred by : Dr. Dighore
Consulted by : DR MUJAWAR MS. DNB

UGISCOPY

Premedication : LOX 4%SPRAY
Esophagus : Normal
OG Junction : 40CMS
Stomach :
Fundus : Mucosa - Gnflammation (+)
Body : Mucosa - Inflammation (+)
Antrum : Severe gastritis.
Pylorus : Normal
Duodenum :
D1 : Normal
D2 : Normal
Impression : SEVERE PAN GASTRITIS

Figure 5. Upper gastrointestinal endoscopic (UGIscopy) study report of a PG student (accident victim).

injection [ondansetron injection (antiemetic)] (Figure 3, Figures S1 and S2). After keeping her under observation for 24 h, she was discharged the next day (February 17, 2022, at 12:15 pm), and the doctor prescribed her a 4 mg Vomiover tablet [Ondansetron (antiemetic)], Pantovel D [domperidone and pantoprazole (to control acidity and nausea)], Betnesol K tablet [Betnesol (antiallergic)], and Zerodol tablet (aceclofenac and paracetamol combination) (Figure 3, Figures S1 and S2) and suggested that she take lighter meals. I assumed that everything was fine and that she was no longer in danger.

On the same day (February 17, 2022, at 4:00 p.m.), I received a call from her, stating that she had nose bleeding and nausea and vomiting that were so severe that she could not even drink water. Hearing from her made me very nervous; we immediately transferred her to the Indira Gandhi Multispeciality (IGM) hospital in the city (it is one of the major hospitals in the city). I discussed everything with Dr. Dighore, the head of the IGM hospital. He had admitted her into the emergency ward of the hospital and started investigating the chemical toxicity. Our entire research team was waiting outside the emergency ward, and in the meantime, I began searching for previously published cases involving acryloyl chloride accidents. Shima et al. reported "acute respiratory distress (ARDS) syndrome" due to acryloyl chloride inhalation in a 36 year-old man who was accidentally exposed to the acryloyl chloride.[18] He was admitted to the intensive care unit (ICU) after being diagnosed with ARDS. Initially, he was treated with a high-flow nasal cannula and sivelestat sodium. Due to the possibility of a delayed exacerbation, he was later switched to methylprednisolone. The patient's oxygenation gradually improved, and he was discharged on the eighth day of his hospitalization.[18] I became more concerned after reading the Lau et al. report, in which he reported three cases of direct inhalation of acryloyl chloride (96%) and methacrylic anhydride (94%).[19] Out of the three cases, one of the student died due to pulmonary edema. The doctor tried *N*-acetylcysteine and steroids; however, his noncardiogenic pulmonary edema did not respond, and he died later. Two students (a 31 year-old male student and a 25 year-old female student) in his case report survived this tragedy. These two students had only mild sore throats and eye discomfort.

I had discussed these previously reported cases and the SDS of acryloyl chloride with Dr. Dighore.[18,19] To investigate the breathing issue, he measured her blood oxygen saturation, which was found to be normal (96 SpO_2), and he said that there was no breathing-related issue with her and that everything would be fine. The chest X-ray confirmed that there were no signs of pulmonary edema (Figure S3). Later, he investigated all major

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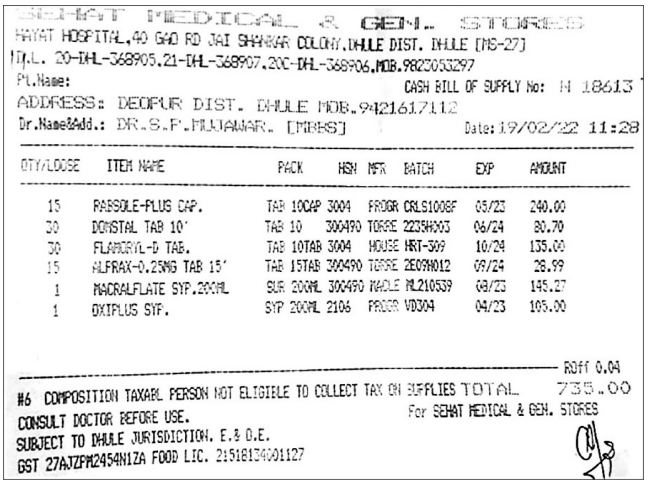
ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

organ toxicities to see how acryloyl chloride affected them. He performed an ECG, and the results were normal (Figure S4).

She complained of nose bleeding in the afternoon; hence, a prothrombin test was performed, and it was found to be normal [12.7 s (normal prothrombin time: 13.09 s)] (Figure 4). To assess liver and kidney function, SGPT and serum creatinine were measured, and both were found to be within normal limits (SGPT, 16 IU/dL; and serum creatinine, 0.89 mg/dL) (Figure 4). Because she was complaining of weakness, serum electrolytes such as sodium, potassium, and calcium were tested. All elements were found to be within normal limits (Figure 4). The hemogram revealed a slight decrease in hemoglobin level (8.6 g %), which was generally observed to be low in females due to menstruation.[23] After all of the biochemical testing, he assured me that there was nothing to be concerned about; however, a further upper gastrointestinal endoscopic (UGIscopy) study is required to determine the cause of persistent nausea and vomiting. He kept her under observation for 12 h and administered a pantoprazole injection (to control acidity) and Betacort injection [Corticosteroid, (antiallergic)] through an IV.

The following day (February 18, 2022), she was referred to Dr. Mujawar in Dhule (Maharashtra, India, 60 km from Shirpur), a well-known gastroenterologist. Dr. Mujawar reviewed the previous reports and advised an upper GI endoscopy (UGIscopy). On February 19, 2022, he performed a UGIscopy at the empty stomach condition of a PG student. The UGIscopy report indicated inflammation of the mucosa of the fundus and body of the stomach, as well as severe gastritis in the antrum area (Figure 5). The duodenum was found to be normal. He concluded that accidental inhalation of acryloyl chloride fumes had damaged the fragile blood vessels of the nose and the mucosa of the GIT (ulceration), resulting in nose bleeding and uncontrollable nausea and vomiting.

Dr. Mujawar stabilizes her acidity, nausea and vomiting, and ulceration in the first round of treatment by prescribing Rabsol Plus capsules (levosulpiride and rabeprazole), Domstal tablet (domperidone 10 mg), Flamoryl-D tablet [diclofenac (50 mg) + paracetamol (500 mg)], Alprax 0.25 mg tablet (alprazolam 0.25 mg), Macralfate Suspension (sucralfate), and Oxiplus syrup (multivitamin) (Figure 6, Figure S5).

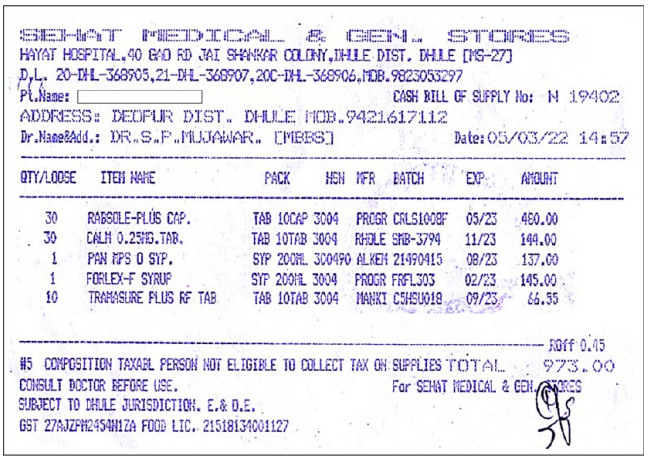

SEHAT MEDICAL & GEN. STORES
HAYAT HOSPITAL,40 GAD RD JAI SHANKAR COLONY,DHULE DIST. DHULE [MS-27]
D.L. 20-DHL-368905,21-DHL-368907,20C-DHL-368906,MOB.9823053297
Pt.Name: CASH BILL OF SUPPLY No: N 18613
ADDRESS: DEOPUR DIST. DHULE MOB.9421617112
Dr.Name&Add.: DR.S.P.MUJAWAR. [MBBS] Date:19/02/22 11:28

QTY/LOOSE	ITEM NAME	PACK	HSN	MFR	BATCH	EXP	AMOUNT
15	RABSOLE-PLUS CAP.	TAB 10CAP	3004	FROGR	CRLS1008F	05/23	240.00
30	DOMSTAL TAB 10'	TAB 10	300490	TORRE	2235H003	06/24	80.70
30	FLAMORYL-D TAB.	TAB 10TAB	3004	MOUSE	HRT-309	10/24	135.00
15	ALPRAX-0.25MG TAB 15'	TAB 15TAB	300490	TORRE	2E09H012	09/24	28.99
1	MACRALFLATE SYP.200ML	SUR 200ML	300490	MACLE	RL210539	08/23	145.27
1	OXIPLUS SYP.	SYP 200ML	2106	PROCR	VD304	04/23	105.00

Roff 0.04
#6 COMPOSITION TAXABL PERSON NOT ELIGIBLE TO COLLECT TAX ON SUPPLIES TOTAL 735.00
CONSULT DOCTOR BEFORE USE. For SEHAT MEDICAL & GEN. STORES
SUBJECT TO DHULE JURISDICTION. E.& O.E.
GST 27AJZPM2454N1ZA FOOD LIC. 21518134001127

Figure 6. First prescription from Dr. Mujawar's hospital of a PG student (accident victim).

In the second round of treatment, Dr. Mujawar prescribed Rabsol Plus capsules (levosulpiride and rabeprazole) (Figure 7,


SEHAT MEDICAL & GEN. STORES
HAYAT HOSPITAL,40 GAD RD JAI SHANKAR COLONY,DHULE DIST. DHULE [MS-27]
D.L. 20-DHL-368905,21-DHL-368907,20C-DHL-368906,MOB.9823053297
Pt.Name: CASH BILL OF SUPPLY No: N 19402
ADDRESS: DEOPUR DIST. DHULE MOB.9421617112
Dr.Name&Add.: DR.S.P.MUJAWAR. [MBBS] Date:05/03/22 14:57

QTY/LOOSE	ITEM NAME	PACK	HSN	MFR	BATCH	EXP	AMOUNT
30	RABSOLE-PLUS CAP.	TAB 10CAP	3004	FROGR	CRLS1008F	05/23	480.00
30	CALM 0.25MG.TAB.	TAB 10TAB	3004	RHOLE	SNB-3794	11/23	144.00
1	PAN MPS O SYP.	SYP 200ML	300490	ALKEM	21490415	08/23	137.00
1	FORLEX-F SYRUP	SYP 200ML	3004	FROGR	FRFL303	02/23	145.00
10	TRAMASURE PLUS RF TAB	TAB 10TAB	3004	MANKI	CSHSU018	09/23	66.55

Roff 0.45
#5 COMPOSITION TAXABL PERSON NOT ELIGIBLE TO COLLECT TAX ON SUPPLIES TOTAL 973.00
CONSULT DOCTOR BEFORE USE. For SEHAT MEDICAL & GEN. STORES
SUBJECT TO DHULE JURISDICTION. E.& O.E.
GST 27AJZPM2454N1ZA FOOD LIC. 21518134001127

Figure 7. Second prescription from Dr. Mujawar's hospital of a PG student (accident victim).

Figure S5). Levosulpiride is a prokinetic drug that works by increasing acetylcholine release and preventing food reflux. Rabeprazole is a proton pump inhibitor (PPI). To alleviate anxiety, Calm 0.25 (benzodiazepine) was given. The Pan MPS is a degasifying preparation that contains aluminum hydroxide (250 mg/5 mL), dimethicone (50 mg/5 mL), and milk of magnesia (250 mg/5 mL). The active ingredients in Forlox M are ofloxacin (50 mg) and metronidazole (100 mg). The Tramasure-Plus RF tablet comprises paracetamol, acetaminophen (325 mg), and tramadol (37.5 mg), which was given to relieve the pain.

She began to feel better after 15 days of Dr. Mujawar's treatment and was slowly recovered from the ulceration phase. After two months of incidents, she has resumed normal eating and digestion.

4. DISCUSSION

This is the third case of an acryloyl chloride accident that we are reporting here.[18,19] The main reason for reporting this accident is to raise awareness among researchers about the lethal consequences of acryloyl chloride, which are fatal and may even result in death, so that PIs and research institutions can implement more stringent controls to reduce exposure. Secondarily, sharing accident information leads to its minimization and avoidance in the future.

There was direct exposure to acryloyl chloride in two previously published reports by Lau et al. and Shima et al.[18,19] Lau et al. discussed three cases in their reports. Case 1 (a male student) died due to pulmonary edema and did not respond to the medication.[19] Case 2 (a male student) and Case 3 (a female student) were also involved in the same accident; however, they only suffered from mild sore throats and eye discomfort, and their chest X-rays were normal. The female student (Case 3) was discharged after 6 h, and the male student (Case 2) was discharged the next day due to some residual cough and throat discomfort.[19]

The case of Sima et al. was of a 36 year-old man who was accidentally exposed to acryloyl chloride.[18] The patient developed dyspnea and wet cough, and his oxygen saturation was 88% at room air. He was diagnosed with "acute respiratory distress syndrome (ARDS)" and admitted to the ICU. Initially,

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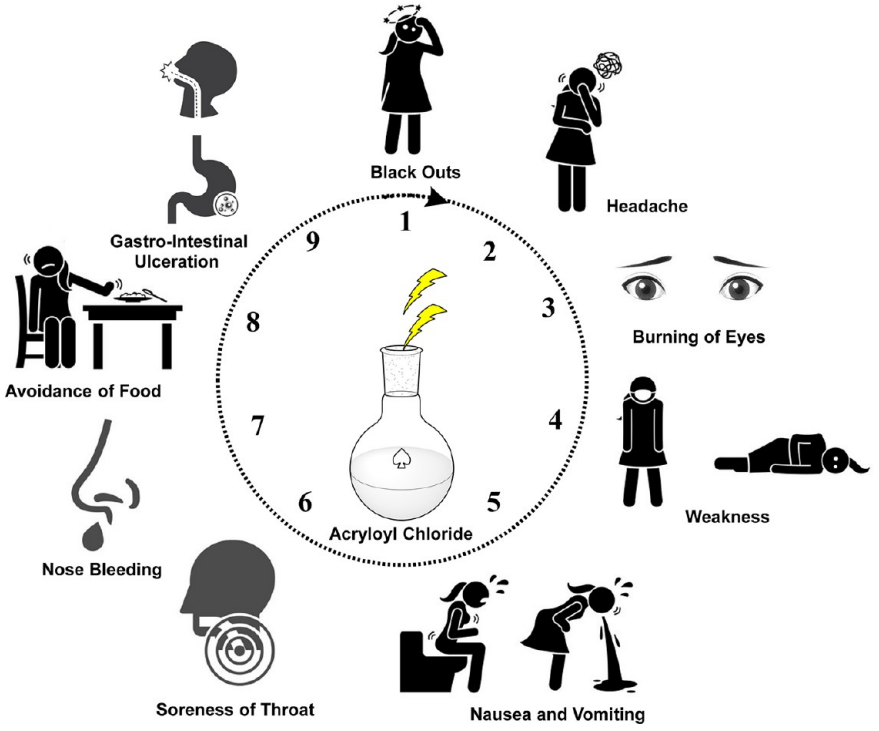

Figure 8. Effects (1−9) of acryloyl chloride on a PG student (accident victim) after accidental inhalation.

he was treated with a high-flow nasal cannula and sivelestat sodium. Later, he was shifted to methylprednisolone due to the possibility of a delayed exacerbation. The patient's oxygenation progressively improved, and he was discharged on the eighth day of hospitalization.[18]

In our case, there was no direct exposure of acryloyl chloride to the victim. It was a reaction mixture (15 mL) with an excess of acryloyl chloride that was bumped while heating the content.

To the best of our knowledge, this is the third report describing exposure to acryloyl chloride,[18,19] and for the first time, we are reporting nose bleeding and stomach ulceration as fatal effects of exposure (not mentioned in SDS). The consequences that happened after the exposure are sequenced in Figure 8. Within 15 min of exposure, the victim experienced headaches, dizziness, blackouts, tiredness, and, most notably, eye burning (Figure 8).

After 4−5 h, nausea and vomiting were prominent, with continued eye burning (even after treatment). On the second day of the incident, she experienced nose bleeding, throat soreness, and intensified vomiting (without food and water, no nausea and vomiting were observed, but as she was taking little water, the content was expelled outside). She had no desire for food. On the third day, she was diagnosed with stomach ulceration.

5. LESSON LEARNED FROM THE ACCIDENT

It would have been desirable if the accident had never occurred; however, it happened, and the most important thing at this point is to assess what we can learn from it and what precautions we can take to prevent anything similar from happening again in the future.

I am grateful to the PG student (accident victim) for allowing this incident to be shared in this Case Study; she wanted the circumstances of the accident to be shared as widely as possible to alert others about the severe consequences of acryloyl chloride. She has not let the accident deter her, and she joined the lab on April 1, 2022, almost one and a half months after the incident, and completed all the pending research projects. The PG student (accident victim) and I would like to share the precautions while carrying out the reaction and informative outlines for the emergency room and doctors, which could be an important lesson (Sections 5.1−5.3) for all researchers to minimize the chances of something similar happening again.

5.1. Precaution while Carrying out the Reaction.

1. The acryloyl chloride bottle comes in a tightly sealed container with a strong rubber cork. It should be stored in a dry, cool, and well-ventilated environment.
2. To avoid skin exposure, this reaction should be carried out while wearing protective eyeglasses or chemical safety goggles, a helmet, a mask, and protective gloves and clothing.
3. Ensure that eyewash stations and safety showers are easily accessible from the workstation. Check for adequate ventilation, especially if you are working in a cramped space.
4. Measuring the acryloyl chloride is a very difficult task while setting the reaction. A suitable long needle with good strength should be used to take out the acryloyl chloride from the sealed rubber cork. This reaction is an exothermic reaction, and hence, it should be carried out in a closed flask with a stopper (iodine flask) (not mentioned in SDS) at 0−5 °C.
5. As a precaution, ammonia solution can be sprinkled around the bottle of acryloyl chloride while drawing it from the bottle to neutralize the fumes (not mentioned in SDS).
6. This reaction should not be carried out during the daytime (when the outside temperature is usually high, more than 25 °C in Asian countries). The preferred time is in the morning or evening when the outside

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ACS Chem. Health Saf. XXXX, XXX, XXX−XXX

temperature is lower than during the day (not mentioned in SDS).
7. The reaction should be worked up carefully, and the filtrate should be properly disposed of outside the lab rather than thrown into the basin because unreacted acryloyl chloride may cause problems for lab mates (eye irritation and suffocation) (not mentioned in SDS).
8. This reaction should not be set single-handedly. Two to three lab members must be present while setting the reaction, and the research supervisor must be present until the reaction is completely worked up (not mentioned in SDS).
9. Such a reaction should not be carried out in UG or PG laboratories, which are usually crowded with students, because acryloyl chloride fumes may also affect them.

5.2. First Aid, Precautions, and Suggestions for the Emergency Room after the Accident. The first symptoms that usually appear are burning eyes and weakness. As a result, the victim's contaminated clothes should be removed, and their eyes and exposed skin should be irrigated with plenty of water.

1. The victim should be rescued immediately and taken to a clean, well-ventilated location. Ensure adequate ventilation. Keep people away from and upwind of the spill or leak.
2. After the initial exposure, the most noticeable symptom is the burning of the eyes. If the chemical gets into your eyes, rinse them thoroughly with water for at least 15 min, including underneath the eyelids, and seek medical attention.
3. If it encounters your skin, immediately wash the affected area with plenty of water (at least for 15 min) and seek medical attention.
4. If the victim has inhaled the chemical and is not breathing, give artificial respiration. Do not use the mouth-to-mouth method if the victim has consumed or inhaled acryloyl chloride.
5. If acryloyl chloride is accidentally consumed, do not induce vomiting. According to the SDS, using gastric lavage or emesis is not recommended because acryloyl chloride may damage delicate tissue and increase the risk of perforation.

5.3. Information and Suggestions for the Doctor. After first aid, the victim should be immediately shifted to the hospital, and associated personnel should show the SDS to the doctor. The severity of the accident can be determined by the signs and symptoms. According to our experience and the previous two reports,[18,19] breathing problems should be treated as a serious sign, while eye burning, tiredness, and throat soreness should be considered moderate levels of the accident. Patients with chest signs, radiological abnormalities, or impaired oxygenation should be admitted to the ICU of the hospital. It may be preferable to begin steroidal therapy at the start of treatment to avoid further aggravation of unintended consequences in addition to symptomatic treatments.

6. LABORATORY ACTION PLAN

After the accidental exposure of acryloyl chloride to a PG student, we developed a standard operating protocol for the safe handling of acryloyl chloride. A separate fume hood was allocated for carrying out this reaction, which was equipped with a waste container and a strong syringe to take out the acryloyl chloride. According to the guidelines, acryloyl chloride should be transferred directly from the cool storage to the fume hood, and the entire reaction setup should be done inside the fume hood. This reaction should not be performed single-handedly, and the support of PI/colleagues must be utilized. When working with acrylation reactions, a PPE kit consisting of a helmet, eye protection, lab coat, and disposable gloves should always be worn. We began providing safety training to all new members who joined the lab following this incident, and special interaction with the PG student (accident victim) has been arranged with them to make them aware of the accidental hazard.

The Laboratory Safety Officers (LSOs) recommended that sub-LSOs should conduct regular lab tours. Simultaneously, we have instructed the IT person to keep an eye (CC TV) on the researcher to see if they are adhering to all safety regulations (like wearing a PPE kit and disposing of the chemicals in the lab basin).

7. CONCLUSION

Acryloyl chloride should be handled with extreme caution. Wearing a PPE kit is very essential, and it should be worn throughout the time of reaction. Burning of the eyes, soreness of the throat, and weakness are the general symptoms that appear after acryloyl chloride exposure, but respiratory distress indicates a high level of severity. Such a patient with respiratory discomfort should be immediately shifted to a well-ventilated area and then to the hospital. Try not to panic, and notify your PI or colleagues as soon as possible; do not assume that this is a temporary situation and that you can handle everything. The support of your PI or colleagues is critical at this point. This reaction should not be performed during the summer, especially in Asian countries where temperatures generally exceed 30 °C. It is disheartening to report that safety information about the reagent is not typically published by any journal. It should be made mandatory to include safety information and possible risk assessment analysis of chemicals and reagents in manuscripts, which may be useful to other researchers. We would like to convey a message to all students, researchers, professors, and safety officers in academia and industry that, when dealing with acryloyl chloride, one must be very cautious and follow all safety norms to protect themselves and the chemistry field. We hope that this accident story will prevent other researchers from becoming victims of acryloyl chloride.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.chas.2c00036.

Prescriptions and medical reports (PDF)

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Complete contact information is available at: https://pubs.acs.org/10.1021/acs.chas.2c00036

Notes

Informed consent was obtained from the victim of this accident. The views expressed in this Case Study are of the authors. The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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