# Netaji Nagar College For Women

Details of Students who completed **Project Work** in fulfillment of

the requirements for the **Dissertation** of

Semester VI Chemistry Honours (CBCS)

**Paper CEMA DSE B-4**

of the University of Calcutta, 2023.

| Serial No. | Name | Roll Number | Registration Number | Period of Project | Title of Project |
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| 1 | Deepa Ray | 203056-11-0032 | 056-1211-0135-20 | January to June 2023 | Aspirin, The Pain Relief Medicine |
| 2 | Riya Kumari Singh | 203056-11-0031 | 056-1211-0134-20 | January to June 2023 | Nitrogen Dioxide in Green Chemistry |

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# CERTIFICATE

This is to certify that Miss Deepa Ray

of BSc Semester VI (CBCS) Chemistry Honours

of this college has completed the project work

titled "Aspirin, The Pain Relief Medicine"

in fulfillment of the requirements for the

Dissertation of CEMA DSE B-4 Course

of the University of Calcutta,

during the period January to May 2023.

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# University of Calcutta

**BSc Semester VI Honours (CBCS) Examination 2023**

**Paper CEMA DSE B-4 (Dissertation)**

# "Aspirin, the Pain Relief Medicine"

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# ACKNOWLEDGEMENT

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Finally, I would like to acknowledge the contributions of my family and friends, who have been a constant source of encouragement and support throughout my journey.

# CONTENTS

**Abstract :-** Pain is a signal in our nervous system that something may be wrong. it is an unpleasant feeling as a prick, tingle, sting, burn or ache. It may be sharp or dull.it may come and go or it may be constant. There are two types of pain: acute and chronic. Acute pain usually comes on suddenly, because of a disease, injury, or inflammation. It can often be diagnosed and treated. It usually goes away, though sometimes it can turn into chronic pain. Chronic pain lasts for a long time, and can cause severe problems. Pain relievers are just one part of a pain treatment plan. Pain relief medicines are used as part of a strategy to manage acute and chronic pain. They work by targeting the cause of the pain or by reducing the feeling of pain. Some pain relief medicines like paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, aspirin or diclofenac.

Aspirin is a non-steroidal anti-inflammation drug, or NSAID, commonly used to treat both acute and chronic pain conditions. Aspirin is available in both over-the-counter and prescription strengths, and can control fevers, or is an antipyretic, as well as treat mild to moderate pain. Aspirin has long been thought to inhibit prostaglandins in the body, which can help relieve some types of pain. It works by stopping the production of certain natural substances that cause fever, pain, swelling, and blood clothes. It is in a group of medications called salicylates.

# PAIN RELIEF MEDICINES

Pain relievers treats variant types of problems. It helps to reduce pain from arthritis, headache and muscle stains. Pain relivers reduce the pain from illness, injury, surgical procedures. Everyone in their life experiences pain differently. Pain may come on suddenly but it can take more time to relief but does.

Pain relivers have many names:

# Analgesics

# Narcotics

# Painkillers

# Pain medicine

## Types of pain relivers -

**Over-the-counter :-** OTC drugs reduces pain from arthritis, headaches and muscle pain. These medication are available at stores. Any adult person can buy them without any prescription.

**PRESCRIPTION :-** prescription painkillers provide stronger relief from chronic pain or severe pain after surgery. These medications are only available with a prescription from a healthcare provider.

### TYPES OF OVER-THE-COUNTER PAIN RELIEVERS

Common OTC pain medications –

**ACETAMINOPHEN :-** This is a pain reliever and a fever reducer. It is used to treat mild pain like slightly headache, muscle aches, arthritis, cold and tooth aches etc.

**NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) :-** This types of drugs are widely used to relieve pain, fever, headache, and reduce

inflammation. It includes **ASPIRIN, IBUPROFEN,** and NAPROXEN compound.

**COMBINATION :-** A combination drug contain two or more drugs in a single dosage. Some pain relievers contain both acetaminophen and aspirin ( an NSAIDs).

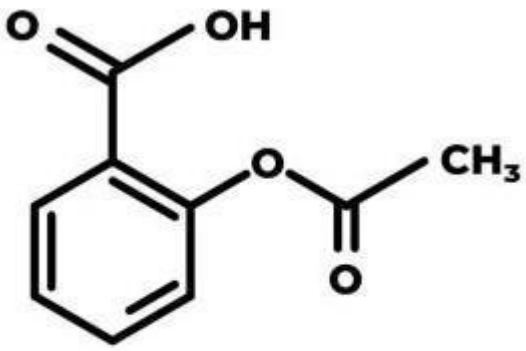
**TOPICAL :-** We apply this pain medication directly to our skin. It can used to treat pain or other problems in specific parts of the body. They may contain aspirin and other medication. It comes as a cream, gel, spray etc. they can also be used to nourish the skin and protect it.

## NON STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) :-

Nonsteroidal anti-inflammatory drugs (NSAIDs) are medicines that are widely used to relieve pain, reduce fever. They also help in relieve headache, body aches, cold flu.

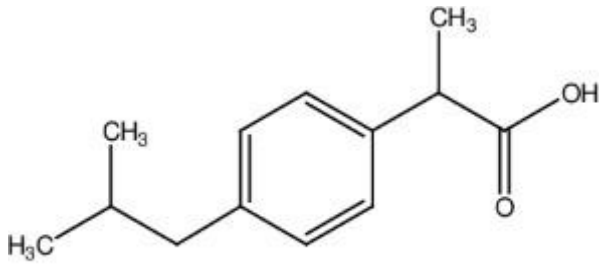
The most common NSAIDs are :-

**ASPIRIN :-** It is also known as acetylsalicylic acid which is used in reduce pain, fever. It can also help for reduce the risk of serious problems.



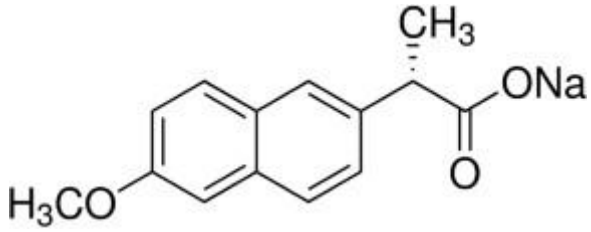

**Aspirin**

**IBUPROFEN :-** It works by reducing hormones that cause inflammation and pain in the body. It is used to reduce fever and treat pain like toothache, back pain and injury.




Ibuprofen

**NAPROXEN SODIUM :-** It is used to treat pain, menstrual cramps, inflammatory diseases such as rheumatoid arthritis and fever. It is taken orally.




naproxen sodium

# DISCOVERY OF ASPIRIN

**INTRODUCTION :-** Aspirin is synthesis by Hoffman of Bayer Laboratories in Aspirin. It is an effective analgesic (Pain reliever), antipyretic (fever reducer) and anti-inflammatory agent. It has become one of the most successful and one of most widely used non-prescription drugs. The story of the discovery of aspirin extend back more than 3500 years to when bark from the willow tree was used as a pain reliever and antipyretic. The active ingredient in Willow bark was later found to be Salicylic acid, which would later from the basis of the discovery of aspirin. The use of willow bark for pain relief continued through ancient Greece, where it was recommended by Hippocrates to relieve the pain of childbirth, through to Roman times, when its use was recorded by Pliny the Elder. Many traditional therapies were used for pain relief over the following centuries but were not studied systematically. In 1899,the Bayer company in Germany modify the salicylic acid and patented a drug known aspirin .

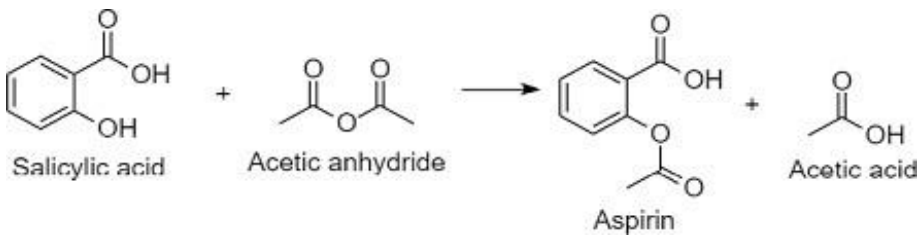
Three key figures in the discovery of aspirin at Bayer were Arthur Eichengrun, which was responsible for developing new drugs, Felix Hoffmann and Heinrich Dreser, which was responsible for clinical trials.

In 1897, Eichengrün decided to develop a form of salicylate that did not cause gastric irritation because salicylic acid contains a phenol

group, and phenols are known to be irritation. So he allocated this task to Hoffmann. Hoffmann had studied as a pharmaceutical chemist at Munich University. Upon being allocated this task.

Felix Hoffmann (1868–1946).

Hoffmann set to work trying to manipulate the salicylic acid that he extracted from dry meadowsweet leaves. He was able to acetylate a phenol group of salicylic acid. [1,2] His breakthrough was recorded in his laboratory book on 10 august 1897. When salicylic acid is heated with acetic anhydride for 3 hour under reflux. The salicylic acid is quantitively acetylated…by its physical properties; e.g. its sour taste without being corrosive, the acetylsalicylic acid differs favourably from salicylic acid, and it is now being tested in this respect to test its usefulness.



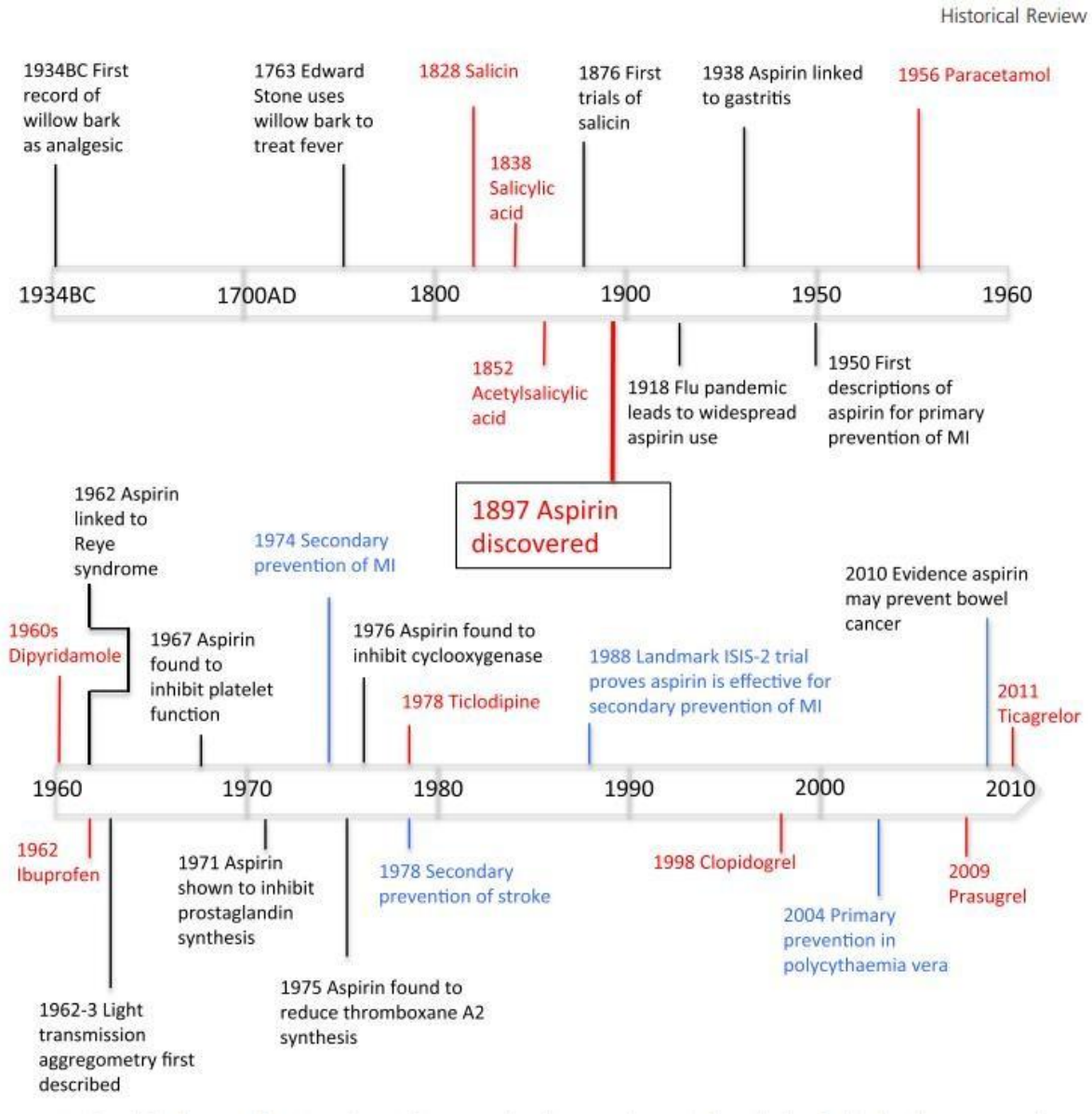

The acetylsalicylic acid (known as aspirin) was put through clinical trials by Dresser's pharmacology division. Initial reports were that it was a successful antipyretic but Dresser rejected it on the grounds that it may cause tachycardia and palpations. Eichengrun did not accept the rejection from the head of the pharmacology division and pushed ahead to run his own clinical trials,

Arthur Eichengrun (1867–1949).

including taking the drug himself. These trials demonstrated it was an effective analgesic and had no apparent adverse effects on the heart. However the intervention of the head of the unit who ordered further trials. Dresser accepted that the drug should be produced.

The name aspirin was agreed by a committee those who had discovered the drug. The name was derived from a combination of

acetyl and spiraea (the Latin name for meadow sweet). Although the uptake of aspirin in the medical community was initially slow, it soon took off and aspirin rapidly become known worldwide as one of the first analgesics. It has been used for the treatment of acute and chronic pain, arthritis and more problems. Despite optimism about the potential role of aspirin in cancer prevention. No other drug is used by a greater number of people worldwide than aspirin. Its yearly use exceeds 45000 tons and americans ingest about 80 million aspirin tablets each day. Regular aspirin use prevents thousands of deaths and hundreds of myocardial (MI) and strokes.

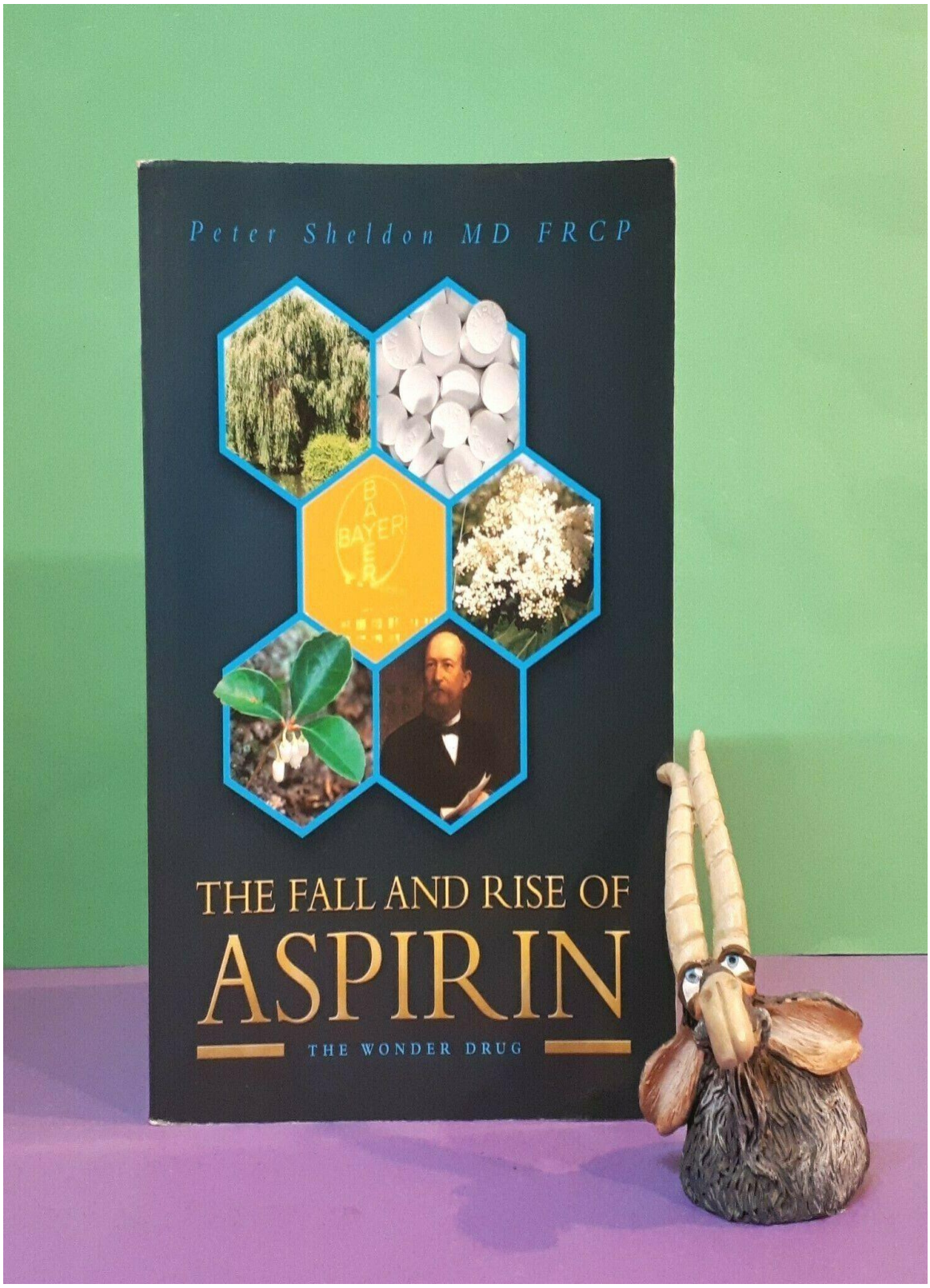


## CONTROVERSY OVER THE DISCOVERY OF ASPIRIN

Eichengrun did not accept the rejection from the head of the pharmacology division and pushed ahead to run his own clinical trials, including taking the drug himself. These trials demonstrated it was an effective analgesic and had no apparent adverse effects on the heart. Dreser was not impressed and wrote a famous note in the margin of Eichengrun's report: 'This is the usual Berlin boasting. The product has no value'. However following the intervention of the head of the unit who ordered further trials, Dreser accepted that the drug should be produced.

The name aspirin was agreed by a committee of those who had discovered the drug. The name was derived from a combination of acetyl and spiraea (the Latin name for meadowsweet). Although the uptake of aspirin in the medical community was initially slow, it soon took off and aspirin rapidly became known worldwide as one of the first analgesics. While Hoffmann and Eichengrun received no royalties for the development of aspirin, Dreser was paid royalties on every medication in his laboratory, and went on to make a personal fortune from the development of aspirin . Although Felix Hoffman is widely credited with the discovery of aspirin, there is some controversy over his claim. At the time of the discovery, Bayer was producing large numbers of new drugs and no individual was specifically credited with the discovery. This changed in 1934, when Schmidt wrote a history of the discovery of aspirin after trawling through the Bayer archives (Schmidt, 1934). Notably, Eichengrun's contribution to the discovery was omitted. Eichengrun was a Jew and the rise of the Nazi party in Germany may have limited his ability to make a claim to a role. He had, by this time, left Bayer to set up his own company but was faced with heavy restrictions on his work. In 1938 he was forced to sell his business and in 1944 he was sent to the Theresienstadt concentration

camp where he remained until the Russians liberated it in 1945. In 1949, 15 years after the publication of the report attributing the discovery to Hoffmann, Arthur Eichengrun, published a manuscript emphasising that the work was performed under his direction. He went on to point out that he identified acetylsalicylic acid as the best compound they had isolated and was the first to call for clinical trials. He reported he had tested it on himself and had initiated the first trials. These trials demonstrated the antipyretic and analgesic effects of acetylsalicylic acid as well as its favourable side effect profile.


Peter Sheldon MD FRCP
BAYER
THE FALL AND RISE OF
ASPIRIN
THE WONDER DRUG

# THE RISE OF ASPIRIN

Within 3 years of its release onto the market, more than 160 scientific papers had been published extolling the virtues of aspirin. It went on to become enormously successful around the world. In 1918 following World War I, the world was hit by another tragic event, a worldwide outbreak of influenza. Approximately 50 million people died from the outbreak: more than died from fighting in the whole of World War I . No cure could be found and vaccination was unsuccessful. Aspirin became widely used and was efficacious in relieving the symptoms of influenza, although it was not effective in reducing mortality. Its popularity was maintained thereafter and aspirin went on to be considered by the public and the medical profession as an effective antipyretic and analgesic, with few side effects when taken at standard doses.

# GENERAL MECHANISM OF ACTION

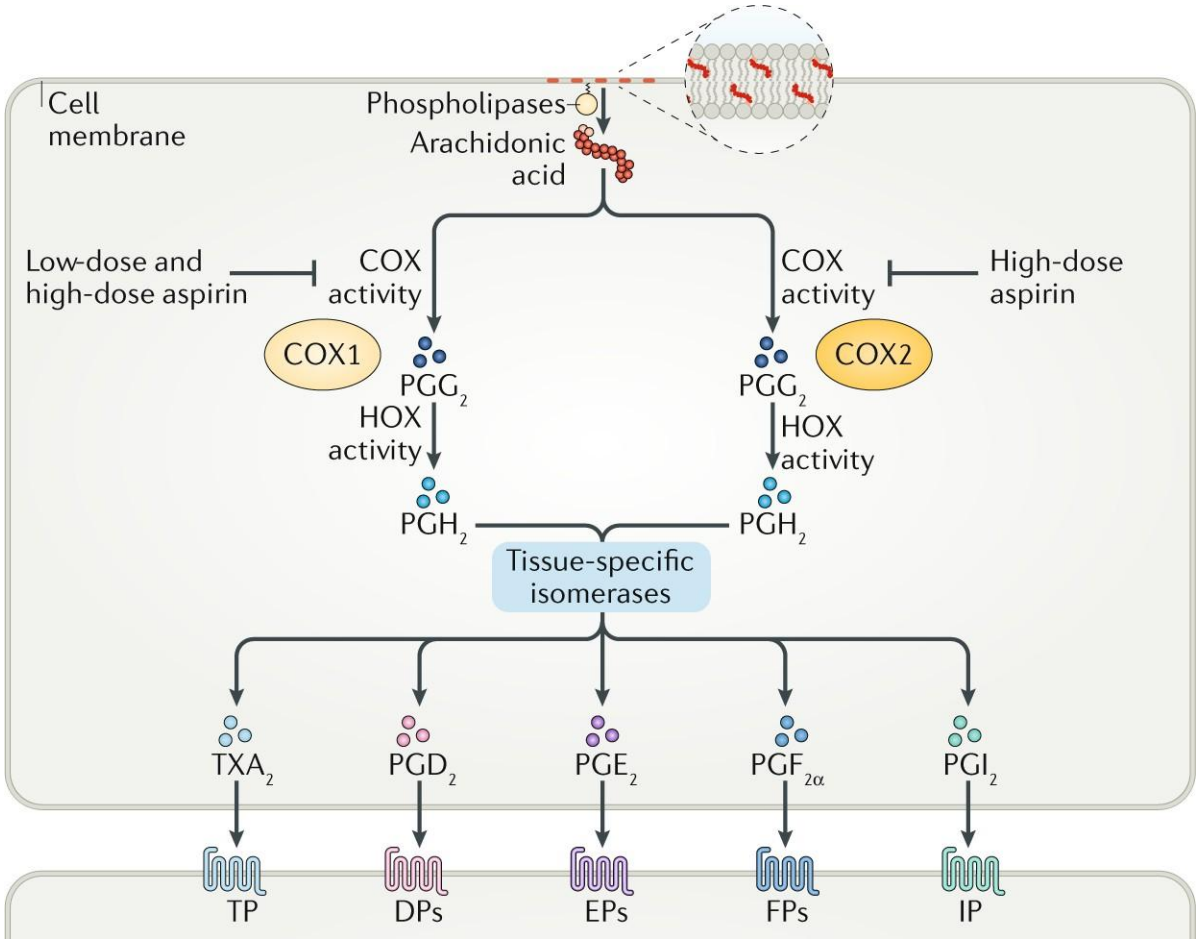
Although universally accepted as an effective pain relieve and fever-reducing agent, before 1971 the workings of this small white tablet remained elusive to scientific investigation. The molecular mechanism that defines aspirin and other NSAIDs as a class is their ability to block the metabolism of arachidonic acid through the prostaglandin H (PGH) synthase or cyclooxygenase (COX) pathway. Inhibition of COX activity decreases the formation of downstream tissue-specific signalling lipids known as prostanoids. These prostanoids include prostaglandin (PG)$D_2$, $PGE_2$ and $PGF_2$, prostacyclin ($PGI_2$) and thromboxane A ($TXA_2$). $TXA_2$ is the major metabolite in platelets that promotes the activation and aggregation of platelets, vasoconstriction, and the proliferation of vascular smooth muscle cells. two distinct isoforms of PGH synthase, derived from different genes, have been identified and designated COX-1 and COX-2. COX-1 is constitutively expressed in most tissues and has a central role in platelet aggregation and gastric cytoprotection. COX-1 is the only isoform present in mature platelets where it is the source of $TXA_2$; COX-2 is constitutively expressed in several tissue (vascular endothelium, kidney and brain) and expression is induced in other tissue during inflammation, wound healing, and neoplasia. COX-2 is the main source of $PGI_2$ in the vascular endothelium. A splicing variant of COX-1 mRNA has been identified that is occasionally referred to as COX-3; however, there is little evidence of a functional COX-3 enzyme in humans.

Although aspirin shares the same molecular targets as other NSAIDs, it differs importantly in how it inhibits the COX isozymes. Whereas aspirin irreversibly inactivates COX-1 and COX-2 through selective acetylation of a critical serine residue within the 'COX-channel' , NSAIDs compete with arachidonic acid for reversible binding

to a common docking site within the COX-channel. Thus, recovery of COX activity after treatment with aspirin requires de novo synthesis of the enzyme, whereas inhibition by other NSAIDs is reversible. Mature platelets, which contain only COX-1, are particularly susceptible to the long-lasting effects of low-dose aspirin treatment, because they lack a nucleus. Other nucleated cells can resynthesize COX isozymes within a few hours. Platelets also encounter a higher concentration of aspirin during their passage through the portal circulation than the concentration that reaches systemic tissues. The systemic concentration of aspirin is 50% lower than in the portal circulation and decreases rapidly because of metabolism by liver and plasma esterases. Thus, the typical aspirin regimen for cardioprotection (once daily administration of 75-100 mg) has negligible and transient effects on extra-platelet targets. Anti – inflammatory doses of aspirin do achieve sufficient systemic concentrations to inhibit COX-2 as well as COX-1 activity, but this inhibition can only be maintained in nucleated cells by repeated dosing three or four times daily.

Direct inhibition of COX-2 activity is the main mechanism by which aspirin and other NSAIDs have been proposed to inhibit the development of certain cancers, although other mechanisms have been hypothesized, as discussed below. The hypothesis that the effect of aspirin on colorectal cancer is mediated by COX-2 inhibition is also supported by results from an epidemiologic study that found aspirin use was associated with lower risk of colorectal cancers that overexpressed COX-2, but was not associated with lower risk of colorectal cancers that showed weak or absent COX-2 expression. Because low-dose aspirin selectively inhibits COX-1 in platelets, and only marginally and transiently inhibits COX-2, it has been considered implausible that the daily low-dose regimen used to inhibit arterial thrombosis could also effectively inhibit the development and progression of certain cancers. To address this inconsistency, we

hypothesize that the antiplatelet effect of low-dose aspirin might mediate both its cardioprotective and cancer preventive effects.




## THE EFFECTS OF ASPIRIN ON PLATELETS

Platelets were first identified in 1865 by Max Schultze (1825–1874) (Schultze, 1865) and were found to be key to normal haemostasis in 1882 by Giulio Bizzozero (1846–1901) (Bizzozero, 1882). [3,4]In 1961, with the role of platelets in pathological thrombus formation becoming increasingly clear, two Oxford scientists, John Poole and John French, postulated that inhibiting platelet function might be key to treating pathological thrombus formation. At the time, they were not aware of any agents that could successfully inhibit platelet function in vivo (Poole & French, 1961) and it would be several more years before the value of aspirin for preventing platelet

aggregation was realised. In 1966, Armand Quick (1894–1978) noted that aspirin prolonged the bleeding time and noted that this was particularly pronounced amongst people with von Willebrand disease leading him to hypothesise that aspirin and von Willebrand disease may have similar effects.

A new technique, light transmission aggregometry, was developed in the early 1960s (Born, 1962; O'Brien, 1962, 1963) and this provided a tool to investigate aspirin's effects on platelets. In 1967, the US physicians, Harvey Weiss and Louis Aledort, reported that aspirin inhibited platelet function (Weiss & Aledort, 1967). They treated ten normal volunteers with either ten 300 mg capsules of aspirin, taken in divided doses, or the equivalent volume of lactulose. Bleeding time increased and platelet aggregation decreased in those treated with aspirin compared to controls.

It was known that arachidonic acid could induce platelets to release rabbit aorta contracting factor and, using the new tests of platelet function, it was shown that this resulted in platelet aggregation. In 1975, work led by Bengt Samuelsson (1934–) in Sweden demonstrated that rabbit aorta contracting factor was thromboxane A2 and that this was antagonised by the effects of aspirin and indomethacin (Hamberg et al, 1975). This work was augmented by the discovery of cyclo-oxygenase in 1976, which we now know to be the enzyme inhibited by aspirin, leading to impaired synthesis of thromboxane. Thromboxane A2 was known to induce vasodilation and aspirin antagonised this, suggesting a potentially prothrombotic effect. However its antiplatelet effect, which was becoming apparent, outweighed the effects of any vasoconstriction (Patrono et al, 1998). The mechanism of action of aspirin was finally proven more 70 years after its discovery.

## USES OF ASPIRIN :-

Aspirin is known as salicylate and a non steroidal anti-inflammatory drug (NSAIDs). It is used to reduce fever and relieve from pain such as headache, toothaches, arthritis. It works by blocking a certain natural substance in our body to reduce pain.

Clinical trials consistently show that antiplatelet therapy with aspirin dramatically reduces the risk of nonfatal myocardial infarcts (MI), strokes. Aspirin provides benefits to almost all patients. The benefits of aspirin in secondary prevention of coronary heart disease, stroke, or peripheral arterial disease are enormous, in addition to reduction or prevention of a variety of cancers. It is estimated that aspirin is still underused, and that its wider use worldwide could save approximately 40,000 more lives per year. Because of these beneficial effects, simple dosage, low cost, and safety, aspirin has become a wonder drug. Aspirin appears to be unique in its cardioprotective action, because nonselective nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen and naproxen, do not have a substantial impact on cardiovascular diseases. Cardiovascular disease (CVD), principally heart disease and stroke, is the leading cause of death for both males and females in developed countries. Aspirin is the most widely used and tested antiplatelet drug in CVD, and it is proven to be the cornerstone of antiplatelet therapy in treatment and prevention of CVD in clinical trials in various populations. In acute coronary syndrome, thrombotic stroke, and Kawasaki's disease, acute use of aspirin can decrease mortality and recurrence of cardiovascular events. As secondary prevention, aspirin is believed to be effective in acute coronary syndrome, stable angina, revascularization, stroke, TIA, and atrial fibrillation. Aspirin may also be used for patients with a high risk of future CVD for primary prevention, but the balance

between benefits and the possibility of side effects must be considered.

## Clinical Use of Aspirin in Treatment and Prevention of Cardiovascular Disease

**INTRODUCTION :-** Cardiovascular disease (CVD) continues to be the leading clinical and public health problem in developed countries and increasingly so throughout the world. Heart disease and stroke are the two main manifestations associated with CVD. The World Health Organization estimates that CVD will be the leading cause of death and disability worldwide by the year 2020 [5]. Millions of patients worldwide take low-dose aspirin on a daily basis for the treatment and prevention of CVD. By far, aspirin is the most widely tested antiplatelet drug in randomized trials of treatment and prevention of CVD. Despite being one of the most widely used drugs in the 20th century, the benefits of aspirin in CVD have only relatively recently been recognized. This paper aims to provide clinical practice with a review of the evidence related to the use of aspirin for the treatment and prevention of cardiovascular events.

### Treatment in cardiovascular disease

**Therapy for Acute Coronary Syndrome :-** convincing data support the use of aspirin in the acute treatment of acute coronary syndrome (ACS), including ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (NSTEMI) and unstable angina pectoris (UA). [5] For ACS patients, the current American Heart Association/American Collage of Cardiology (AHA/ACG) guidelines recommend that aspirin should be administered as soon as possible with an initial loading dose of 162-325 mg and continued indefinitely

with a dose of 75-162 mg daily. [6] In the second international study of infarct survival (ISIS-2) study, the use of aspirin (162 mg chewed, to ensure rapid therapeutic blood levels) was associated with a 23% reduction of vascular mortality rate in MI patients and close to a 50% reduction of nonfatal reinfarction or stroke, with benefits seen in both men and women. In UA and USTEMI patients, aspirin has been shown to reduce the risk of fatal or nonfatal MI by 50-70% during the acute phase and by 50-60% at 3 months to 3 years.

The highest benefit of aspirin was seen in those undergoing coronary angioplasty, with a 53% ($P<0.0002$) reduction in MI, stroke, or vascular deaths. In percutaneous coronary intervention (PCI), the use of aspirin significantly reduces abrupt closure after balloon angioplasty and significantly reduces stent thrombosis rates.

**Therapy for Kawasaki's Disease :-** Kawasaki's disease, which is a kind of acute vasculitis, occurs most commonly in children and in 15 to 25% of untreated cases results in the development of coronary artery aneurysms. [5,6] In the consensus guidelines from the seventh American Collage of Chest Physicians (ACCP) conference on Antithrombotic and Thrombolytic Therapy, high dose aspirin (80-100 mg/kg/day) is recommended during the acute phase of the illness for its anti-inflammatory effects, followed by low-dose aspirin (3-5 mg/kg/day) for its antiplatelet effect for 7 weeks or longer, maintaining it util the patient shows no evidence of coronary changes. In children with warfarin and low-dose aspirin is recommended.

**Therapy for Thromboembolic stroke :-** With regard to stroke, the International Stroke Trial (IST) and the Chinese Acute Stroke Trial (CAST) together enrolled more than 40,000 patients admitted to hospital within 48 hours of the onset of stroke symptoms, who were randomized within 48 hours of the onset of symptoms to 2 to 4 weeks of daily aspirin therapy or placebo. Results from both trials suggest that aspirin therapy decreased the risk of recurrent stroke and death without significantly increasing the risk of hemorrhagic stroke[5,6].

These results are consistent with biochemical evidence of episodic platelet activation during the first 48 h after the onset of symptoms of an acute ischemic stroke and with suppression of in vivo TXA2 biosynthesis in patients receiving low-dose aspirin in this setting.

## SECONDARY PREVENTION

Secondary prevention refers to the use of aspirin to prevent cardiovascular and cerebrovascular events in patients who have already experienced such an event or who have a high risk of an event. Long-term aspirin therapy reduces the yearly risk of serious vascular events (nonfatal myocardial infarction, nonfatal stroke, or vascular death), which corresponds to an absolute reduction of nonfatal events and to a smaller, but still definite, reduction in vascular death. Against these benefits, the absolute increase in major gastrointestinal or other major extracranial bleeds is relatively smaller. Hence, for secondary prevention, the benefits of aspirin therapy substantially exceed the risks, and aspirin is recommended as secondary prevention in conjunction with lifestyle change and stopping smoking to reduce an individual's overall risk of further cardiovascular events. These highrisk patients, including acute MI, acute stroke, previous stroke or transient ischemic attack (TIA), peripheral arterial disease, atrial fibrillation, antiplatelet therapy reduced the combined outcome of any serious vascular event by about 25%, reduced nonfatal myocardial infarction by about 33%, reduced nonfatal stroke by about 25%, and reduced vascular mortality by about 17%. In each of the high-risk categories, the absolute benefits outweighed the absolute risks of major extracranial bleeding.

For the choice of aspirin dosage, this analysis showed that COX is virtually completely inhibited in platelets, producing an antithrombotic effect.Low-dose aspirin (75–150 mg daily) is an effective antiplatelet regimen for long-term use, and the effects of

doses lower than 75 mg daily were less certain. In clinical acute settings requiring an immediate antithrombotic effect (such as acute myocardial infarction, acute ischaemic stroke, unstable angina), an initial loading dose of about 150–300 mg aspirin should probably be given. Aspirin (or another oral antiplatelet drug) is protective in most types of patient at increased risk of occlusive vascular events, including those with an acute myocardial infarction or ischaemic stroke, unstable or stable angina, previous myocardial infarction, stroke or cerebral ischaemia, peripheral arterial disease, or atrial fibrillation.

**Secondary Prevention for Acute Coronary Syndromes :-** The benefit of aspirin therapy for preventing cardiovascular events in patients with ACS (STEMI, USTEMI, UP) has been definitively demonstrated in several trials. The previous meta-analysis by the ATT Collaboration reviewed 18788 patients with a history of MI from the 12 most important randomized clinical trials of aspirin and showed that aspirin therapy reduced the relative risk of nonfatal MI by 28% ($P < 0.0001$), vascular death by 15% ($P < 0.0006$), and overall mortality by 11% ($P = 0.02$) [5,6]. The daily dosage appears to be effective in reducing the risk of cardiovascular events.

The 2007 ACC/AHA guidelines for the management of patients with unstable angina and non-ST-segment elevation MI recommend initiating daily aspirin therapy with at least 162 mg as soon as possible after clinical presentation, with 75–325 mg daily indefinitely thereafter. The 2004 ACC/AHA guidelines for the management of patients with ST-segment elevation MI are similar but recommend 75– 162 mg daily as maintenance therapy after ST-segment elevation MI. Aspirin therapy is considered a class I recommendation (evidence supports that treatment is useful and effective) for all acute coronary syndromes. The initial dose of aspirin should be chewed and then swallowed during acute coronary syndromes to attain a rapid onset of action.

**Secondary Prevention for Chronic Stable Angina :-** A subgroup analysis of the US Physicians' Health Study (PHS) of 333 men with chronic stable angina indicated that aspirin reduced the relative risk of acute MI by 87% ($P < 0.001$). The Swedish Angina Pectoris Aspirin Trial involved 2035 patients and found a 34% relative risk reduction in the occurrence of a first MI over a four-year follow-up period in patients receiving 75 mg of aspirin daily, compared with patients receiving placebo [6]. The 2002 ACC/AHA guidelines for chronic stable angina include a class II a recommendation (the weight of evidence where opinion is in favor of usefulness and efficacy) for prophylactic aspirin therapy to prevent MI and death.

**Secondary Prevention for Stroke and Transient Ischemic Attack :-** The previous meta-analysis by the ATT Collaboration involved 18270 patients with a history of stroke or transient ischaemic attack in 21 trials. The result showed that antiplatelet therapy (mainly aspirin alone) for a mean duration of 29 months can significantly reduce the rate of major vascular events by 22%. Treating 1000 patients with a history of cerebrovascular disease for this duration will prevent about 36 vascular events, mostly nonfatal stroke recurrence (25 fewer per 1000 treated), and some nonfatal myocardial infarction (5 fewer per 1000).

## PRIMARY PREVENTION

For primary prevention, the balance between benefits and risks of aspirin use is less clear because the absolute benefits of aspirin are generally lower than those in secondary prevention. Current guidelines largely ignore any differences in bleeding risk and recommend that aspirin be used widely for primary prevention in those at moderately raised risk of coronary heart disease. It has also been suggested that, since age is a major determinant of the risk of

coronary heart disease, daily aspirin should be started in all people above a specific age, either alone or in combination with other drugs. To date, six completed randomized trials have evaluated the benefits and risks of low-dose aspirin for the primary prevention of cardiovascular disease. The British Male Doctors' Trial (BDT) of 5139 male physicians and the US Physicians' Health Study (PHS) of 22071 healthy male were completed during the late 1980s. The Thrombosis Prevention Trial (TPT) of 5085 men and the Hypertension Optimal Treatment (HOT) trial of 18790 (47% women) patients were completed in 1998. The Primary Prevention Project (PPP) study of 4495 (58% women) patients and the Women's Health Study (WHS) of 39876 healthy females were completed in the 2000s. In all these trials patients were randomized to aspirin and had follow-up durations ranging from 3.6 to 10.1 years. The PHS and BDT used aspirin regimens of 325 mg every other day and 500 mg/day, respectively, whereas the TPT and HOT used 75 mg/day of aspirin and the PPP and WHS used 100 mg/day of enteric-coated aspirin. The Antithrombotic Trialists' (ATT) Collaboration undertook a meta-analysis in the 6 previous trials and found that, in the primary prevention trials, aspirin use yielded a 12% proportional reduction in serious vascular events (0.51% aspirin versus 0.57% control per year, P = 0.0001), due mainly to about 20% reduction in nonfatal myocardial infarction. The net effect on stroke was not significant. Vascular mortality did not differ significantly. Aspirin use increased major gastrointestinal and extracranial bleeds, and the main risk factors for coronary disease were also risk factors for bleeding. To better understand the impact of sex on the response to aspirin, Berger and colleagues conducted a meta-analysis on the sex-specific benefits of aspirin in 51342 women and 44114 men enrolled in the 6 previous prevention trials. The results demonstrate that aspirin therapy is associated with a significant reduction in the risk of cardiovascular events in both sexes. However, the specific types of benefit differ in important ways between women and men. Aspirin use in women was associated with statistically significant reductions

in cardiovascular events and ischemic strokes; no statistically significant benefit was found in the reduction of myocardial infarctions or cardiovascular mortality. In men, aspirin use was associated with a statistically significant reduction in cardiovascular events and myocardial infarctions; no statistically significant benefit was found in the reduction of ischemic strokes or cardiovascular mortality. Total mortality was not significantly reduced by aspirin use in men or women. In summary, consistent evidence from randomized clinical trials indicates that aspirin use reduces the risk for CVD events in adults without a history of CVD. For primary prevention of cardiovascular disease, aspirin therapy significantly reduced the risk of the composite of cardiovascular events primarily by reducing the risk of ischemic stroke with no significant effect on the risk of MI in women and predominantly by reducing the risk of MI with no significant effect on the risk of stroke in men.

## ADVERSE EFFECTS

Aspirin prevents thrombotic events by inhibiting prostaglandin synthesis, which also leads to adverse side effects, mainly including upper-gastrointestinal (GI) toxicity, extracranial and intracranial haemorrhage.

Aspirin-induced GI toxicity detected in randomized clinical trials, including nausea, heartburn, and epigastric pain, appears to be dose related in the range of 30 to 1,300 mg/d. The principle mechanism is due to the inhibition of COX-1-dependent prostaglandin E2 (PGE2) synthesis by aspirin, while PGE2 inhibits acid secretion in gastric mucosa and increases mucous formation. Buffered and entericcoated aspirin preparations developed to attenuate local gastric erosion and minimize this side effect.

The overall risk of major extracranial and intracranial hemorrhage associated with antiplatelet drugs is difficult to assess in individual trials because their incidence is low. In the overview of the ATT Collaboration, the overall proportional increase in risk of a major extracranial hemorrhage with aspirin therapy was about one-half. After allowing for noncompliance in the trials, they are compatible with the 2- to 2.5-fold excess observed in case-control studies. The overall absolute excess of intracranial hemorrhage due to aspirin therapy was <1 per 1000 patients per year in high-risk trials, with somewhat higher risks in patients with cerebrovascular disease.

Moreover, chronic large dose of aspirin use may reduce renal blood flow and glomerular filtration and impair renal function due to the inhibition of COX-2-dependent PGI2, which support renal perfusion, diminish vascular resistance, and facilitate natriuresis. This side effect often occurs at high aspirin doses and most frequently in elderly patients and those with established renal disease.

Furthermore, high-dose aspirin may also attenuate the benefit of angiotensin-converting enzyme (ACE) inhibitors in hypertensive and

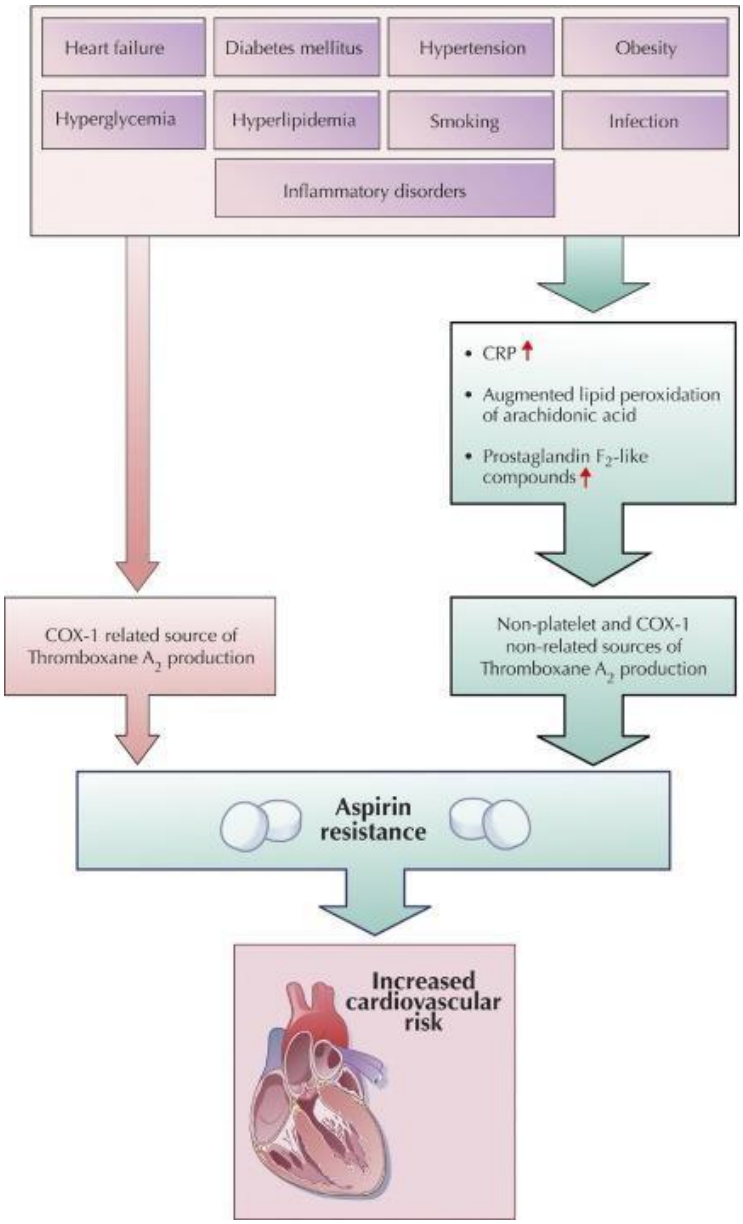
congestive heart failure patients because aspirin may attenuate the synthesis of PGE3 and PGI2, which is promoted by ACE inhibitors.

In summary, aspirin is effective for the prevention of thrombosis because of the inhibition of TXA2-dependent platelet function, which is also associated with excess bleeding. Assessing the net effect requires an estimation of the absolute thrombotic versus hemorrhagic risk of the individual patient.

## ASPIRIN RESISTANCE

Aspirin resistance has been used to describe the inability of aspirin to protect individuals from thrombotic complications, cause a prolongation of the bleeding time, reduce TXA2 production, or produce typical effect in vitro tests of platelet function. However, a standard, clear, and distinct definition of aspirin resistance has not been established yet.

The rate of aspirin resistance is widely variable, ranging from 5 to 60% of the population affected by cardiovascular and cerebrovascular diseases in different studies. It is difficult to know the exact prevalence of aspirin resistance from these studies because of variabilities in definitions for aspirin resistance, variabilities in testing and measurement between studies, small sample size of the studies, and different populations used in the studies. Many laboratory tests are currently used to investigate platelet activity and platelet response to aspirin, such as measurements of thromboxane biosynthesis, platelet aggregation, and platelet activation, bleeding time.




The potential mechanisms of aspirin resistance include enhanced platelet turnover, genetic polymorphisms of COX-1 and other genes involved in thromboxane biosynthesis, upregulation of nonplatelet sources of thromboxane biosynthesis, and the interactions of other drugs.

Because of a series of adverse cardiovascular events associated with aspirin resistance, once aspirin resistance is confirmed by laboratory measures, recommendations for alteration of therapy (dose change or additional antiplatelet agent) and follow up are needed for meaningful clinical outcomes.

## CONCLUSION :-

Aspirin has come a long way since the use of willow bark by the ancient Sumerians and Egyptians. Aspirin is the most commonly used medication worldwide and has proved life saving in the prevention of cardiovascular disease. Scientific discoveries describing the action of aspirin on prostaglandin synthesis and its beneficial effects on inflammation, pain, and fever. The discovery of aspirin and its underlying mechanism also exposed new areas of science and allowed further development of novel antiplatelet agents and anti-inflammatory medications. Soon after the discovery of its antithrombotic qualities, secondary prevention studies suggested a significant benefit with aspirin. However, the exact role of aspirin in primary prevention in still uncertain. An important limitation of the current evidence is uncertainty about the size of the chemo-preventive benefit.

An important first step in future research on this issue is for independent analysts to formally assess the heterogeneity of results between the trials of daily aspirin use and the two large null trials of alternate – day aspirin use.

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# CERTIFICATE

This is to certify that Miss Riya Kumari Singh

of BSc Semester VI (CBCS) Chemistry Honours

of this college has completed the project work

titled "Nitrogen Dioxide in Green Chemistry"

in fulfillment of the requirements for the

Dissertation of CEMA DSE B-4 Course

of the University of Calcutta,

during the period January to May 2023.

[Dr CHAITALI BHATTACHARJEE]

NETAJI NAGAR COLLEGE
Head of the
Dept of Chemistry
FOR WOMEN

# University of Calcutta

**BSc Semester VI Honours (CBCS) Examination 2023**

**Paper CEMA DSE B-4 (Dissertation)**

# "Nitrogen Dioxide in Green Chemistry"

**Name: RIYA KUMARI SINGH**

**Roll Number: 203056-11-0031**

**Registration Number: 056-1211-0134-20**

**Netaji Nagar College for Women**

# CONTENT

# ACKNOWLEDGEMENT

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Finally, I would like to acknowledge the contributions of my family and friends, who have been a constant source of encouragement and support throughout my review journey.

# ABSTRACT

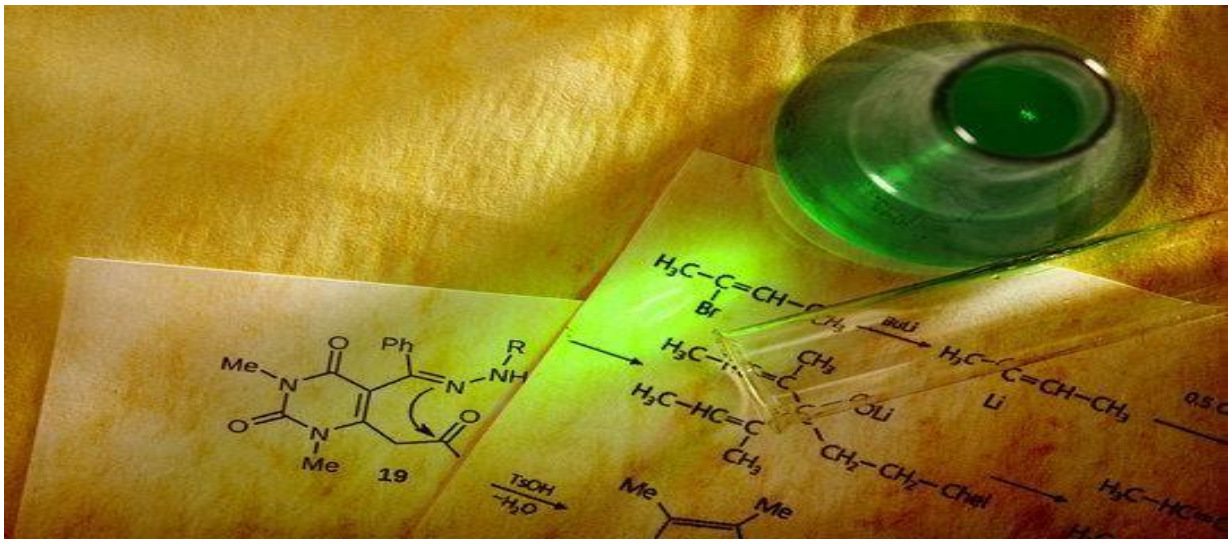
**Nitrogen dioxide ($NO_2$)** is a harmful gas that contributes to air pollution and is a major cause of respiratory diseases. Green Chemistry is a framework for designing chemical processes and products that minimize the use of hazardous materials and reduce waste. In the context of $NO_2$, green chemistry focuses on developing methods to reduce or eliminate the production of $NO_2$ during industrial processes, as well as ways to mitigate its harmful effects on the environment and human health. This can involve using alternative, less hazardous reagents, optimizing reaction conditions to reduce byproducts, and developing efficient catalysts and reactors. Green Chemistry approaches to $NO_2$ have the potential to significantly reduce the environmental impact of industrial processes and improve public health outcomes.

# GREEN CHEMISTRY

Sustainable and green chemistry in very simple terms is just a different way of thinking about how chemistry and chemical engineering can be done. Over the years different principles have been proposed that can be used when thinking about the design, development and implementation of chemical products and processes. These principles enable scientists and engineers to protect and benefit the economy, people and the planet by finding creative and innovative ways to reduce waste, conserve energy, and discover replacements for hazardous substances.

It's important to note that the scope of these of green chemistry and engineering principles go beyond concerns over hazards from chemical toxicity and include energy conservation, waste reduction, and life cycle

considerations such as the use of more sustainable or renewable feedstocks and designing for end of life or the final disposition of the product.



The goal of green chemistry is to create products that are not only safer for the environment and human health but also economically viable.

● **<u>THERE ARE TWELVE PRINCIPLES OF GREEN CHEMISTRY:</u>**

1) Waste Prevention
2) Atom Economy
3) Less Hazardous Chemical Synthesis
4) Designing Safer Chemicals
5) Safer Solvents and Auxiliaries
6) Design for Energy Efficiency
7) Use of Renewable Feedstocks
8) Reduce Derivatives
9) Catalysts
10) Design for Degradation
11) Real – Time Pollution Prevention
12) Safer – Chemistry for Accident Prevention

As we know the main aim of Green Chemistry is reduce the pollution. That's why I mainly focused on the topic of **Prevent Waste**.

# PREVENT WASTE

Waste prevention is defined as use the less amount of toxic waste which are generated at home, work and in our everyday life.

## ● BENEFITS OF WASTE REDUCTION:

1) **Environmental benefits :** Reducing Pollutions
2) **Economic benefits :** Conserving energy and resources
3) **Social benefits :** Improving public health
4) Reduced environment impact such as Green House Effect emission and pollution.

## ● THERE ARE MANY TYPES OF WASTES:

1) Atmospheric wastes
2) Solid wastes
3) Sewage wastes
4) Industrial wastes
5) Agricultural wastes
6) Commercial wastes
7) Domestic wastes
   7.a) Biodegradable wastes
   7.b) Non – Biodegradable
8) Chemical wastes

## ■ WASTES AND THEIR COMPONENTS:

| WASTE | COMPONENTS |
|---|---|
| 1) Atmospheric Waste | Particulate matter, $NO_2$, $SO_2$ |
| 2) Solid Waste | Paper, Cardboard, Glass, Metals |
| 3) Sewage Waste | Chemicals, Heavy metals, Animal Waste |
| 4) Industrial Waste | Radioactive waste, Chemical waste |
| 5) Agricultural Waste | Pesticides, Pharmaceuticals |
| 6) Commercial Waste | Plastics, Textiles, Glass |
| 7) Domestic Waste | Metals, Glass, Hazardous waste |
| 8) Chemical Waste | Heavy metals, Solvents, Acid and bases |

Here I mainly focused on the topic **Atmospheric waste** and write a brief note about it.

# ATMOSPHERIC WASTE

Atmospheric waste is also known as 'AIR POLLUTION'. It refers to the presence of harmful substances and particles in the earth's atmosphere, which have negative effects on human health, environment and climate. Air pollution can be either natural or man – made, and they include gases such as carbon monoxide, Sulphur dioxide, nitrogen dioxide and ozone as well as particulate matter, such as dust, smoke and pollen.

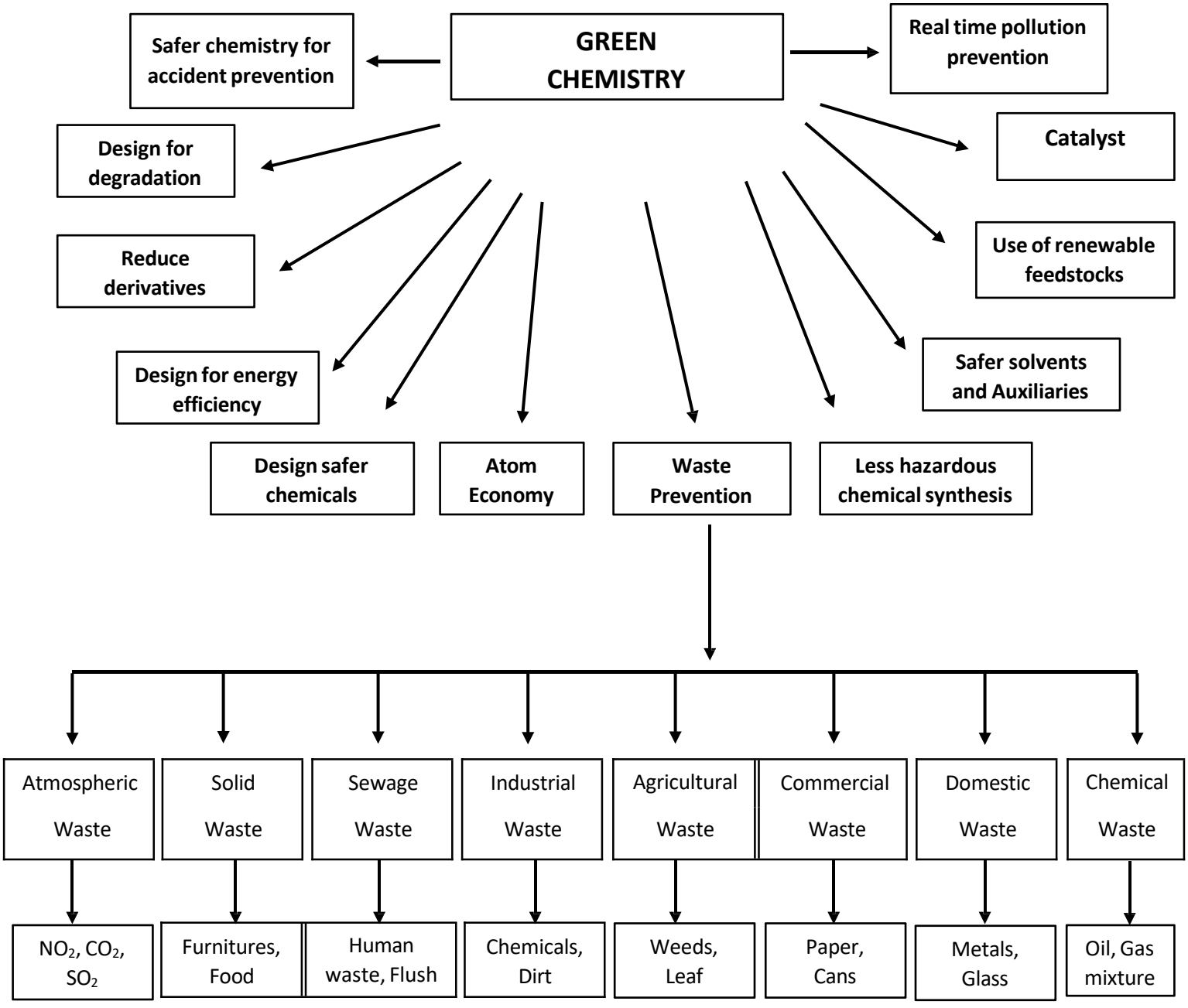
With a variety of sources air pollution can occur, including industrial processes, transportation and agriculture. Fossil fuels, coal, oil and natural gas are the major contributors of Air pollution. They are release large amounts of harmful gases like $CO_2$, $NO_2$ and other greenhouse gases in the atmosphere, as well as other pollutants after burning.

The effects of air pollution on human health can range from mild respiratory irritation to more serious conditions such as asthma, heart disease and cancer. It can also harm the environment by damaging crops, forests and water sources, and by contributing to climate change. Air pollution have economic impacts, including increased healthcare costs and released productivity.

To control the air pollution, governments and organizations started many policies and programs around the world.

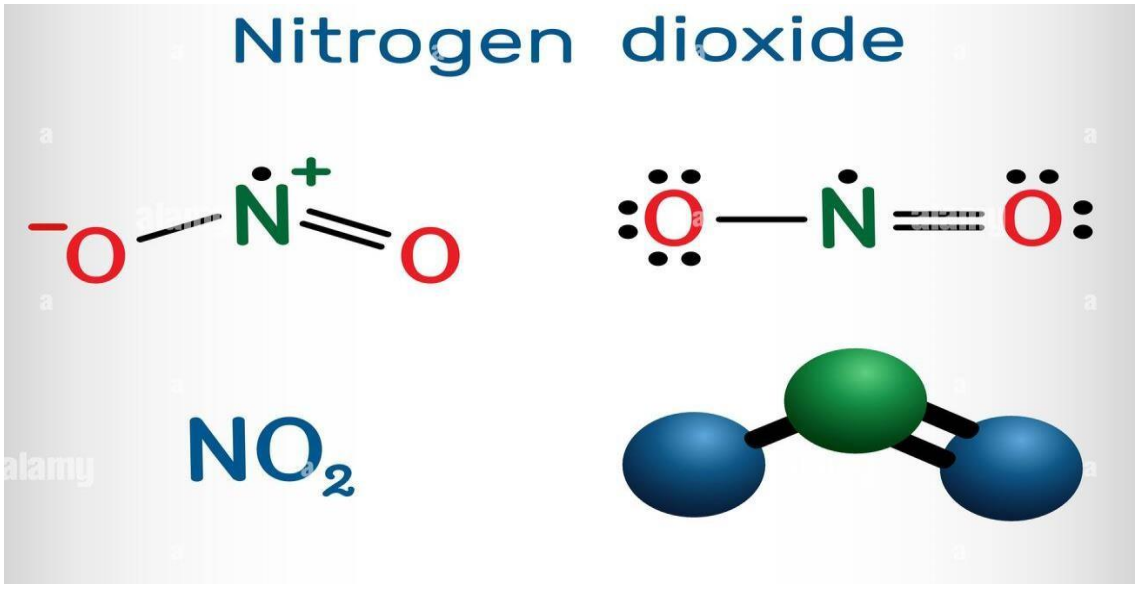
There are many components of Air Pollution but I choose $NO_2$ (Nitrogen dioxide) as my dissertation topic.

## FLOW CHART FROM ABOVE THE DATA



# NITROGEN DIOXIDE

- **INTRODUCTION:** Nitrogen dioxide ($NO_2$) is a highly reactive gas and a harmful air pollutant that is primarily produced by the combustion of fossil fuels in transportation, Power generation, and industrial processes. This gas formed when nitrogen oxide (NO) reacts with oxygen ($O_2$). This reddish brown gas has a pungent odor and is a major contributor to the formation of smog and acid rain. In NO2, there are 2 sigma bonds and 1 lone electron pair. The two oxygen atoms have octet of electrons each. The P orbital of nitrogen forms a $\pi$ – bond with the oxygen atom. Exposure to $NO_2$ can cause many human problems. To control the excessive use of $NO_2$, many countries have implemented regulations and policies.




## BACKGROUND

$NO_2$ is generally considered a useful indicator for measuring and judging air pollution. Epidemiological studies suggest that $NO_2$ enhances short – term effects of a particular matter. Also recent reviews are related to possible effects on human immune system – experimentally animal studies and studies on controlled human exposures suggests that allergenic properties might be enhanced in the presence of $NO_2$. Long – term effects are reduction of lung

function in children and adults can be found in those with higher $NO_2$ exposures.

World Health Organization (WHO) therefore retains short – and long – term guidelines values for $NO_2$ needed to protect population's health and environment.

$NO_2$ is introduced into the environment by natural causes, including entry from the stratosphere, bacterial respiration, volcanos and lightning. These sources make $NO_2$ a trace gas in the atmosphere of earth, where it plays a role in absorbing sunlight and regulating the chemistry of the troposphere, especially in ozone concentrations.

$NO_2$ diffuses into the epithelial lining fluid (ELF) of the respiratory epithelium and dissolves. It chemicals reacts with antioxidant and lipid molecules in the ELF. The health effects of $NO_2$ are caused by the reaction products which are reactive nitrogen species and reactive oxygen species that can drive bronchoconstriction, reduced immune response, and may have effects on the heart.

Interaction of $NO_2$ with water, oxygen and other chemicals in the atmosphere can form acid rain which harms sensitive ecosystems such lakes and forests. Elevated levels of $NO_2$ can also harm vegetative decreasing growth, and reduced crop yield.

Nitrogen dioxide is found in the atmosphere as a key ingredient in photochemical formation of smog and acid rain, nitrogen dioxide is a poisonous has that forms during combustion. Toxic at high concentrations, it reacts with moisture in the air to form nitric acid, highly corrosive and hazardous to plants and animals.

It is an oxidizing free radical which can initiate a variety of destructive pathways in living systems, and several diseases are suspected to be connected with both exogenously and endogenously source of $NO_2$ radicals, but other sources, among them enzymatically ones, have identified recently. It also became clear during the last few years that in vivo formation of 3 – nitro tyrosine strictly depends on the availability of $NO_2$ radicals.

Nitrogen dioxide emissions from diesel and gasoline internal combustion engines have been measured over a range of speed and load condition. $NO_2$ levels are very much higher than expected thermodynamically with as much as 30% of the $NO_x$ emission from a diesel engine at 15% load in the form of $NO_2$.

A recent publication of Ogen (Ogen, 2020) that examined the relationship between long – term exposure to nitrogen dioxide ($NO_2$) can coronavirus fatality raise the very important question on the impact of air pollution on health. Unfortunately, it does not provide sufficient basis for its conclusion that $NO_2$ is "One of the most important contributors to fatality caused by the COVID – 19 virus in these regions and across the whole world." **[Ref – 9]**

Nitrogen dioxide on earth today has biogenic and anthropogenic sources. During COVID – period this is observed that emission of $NO_2$ is decreased in urban areas.**[Ref – 6]** We can take a example that $NO_2$ as an industrial byproduct, we use a one – dimensional photochemical model and synthetic spectral generator to assess the detectability of $NO_2$ as an atmospheric techno – signature on exoplanets. We consider causes of an earth – like planet around sun – like, k – dwarf and M – dwarf stars. We find that $NO_2$ concentrations increase are fewer short – wavelength photons that can photolyzed $NO_2$. In cloud – free results present earth level. $NO_2$ on an earth – like planet around a sun – like star at 10pc. Can be detected with signal to noise ratio approx. 5 within approx. 400 hour with a 15m LUVOIR – like telescope when observed in the 0.2 – 0.7 $\mu m$ range where $NO_2$ has a strong absorption. However, and aerosols can reduce the detectability and could mimic the $NO_2$ feature. From this we can understand how much $NO_2$ is harmful for us or for environment.

## ■ Applications of Nitrogen dioxide in green chemistry:

Nitrogen dioxide ($NO_2$) is a highly reactive gas that is commonly associated with air pollution. However,, it can also be used in green chemistry applications. Here are some examples of it –

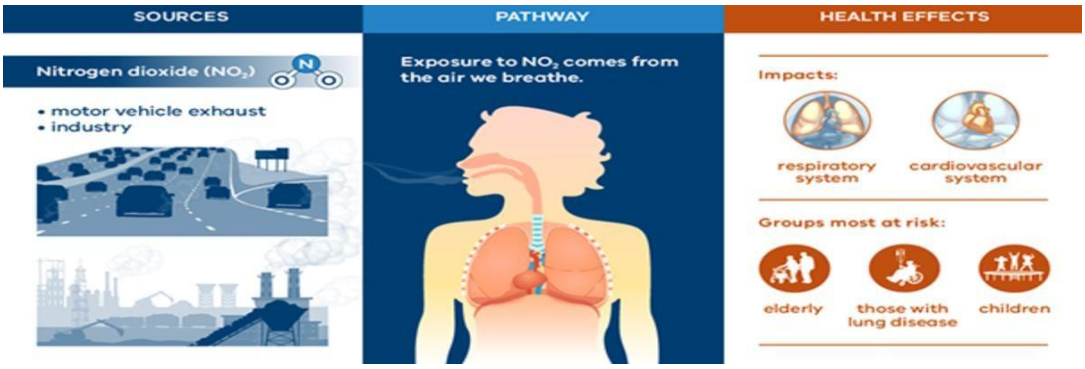
1) **Oxidant:** Nitrogen dioxide is a powerful oxidant that can be used to replace traditional oxidants like permanganate or dichromate in some oxidation reactions. This can reduce the amount of hazardous waste generated.
2) **Nitrating agent:** Nitrogen dioxide can be used as a nitrating agent in the production of certain organic compounds, such as nitrobenzene. This can be a more sustainable than using other nitrating agents that may be more toxic or generate more waste.
3) **Polymerization initiator:** Nitrogen dioxide can be used as a polymerization initiator in the production of certain polymer, such as polyethylene terephthalate (PET). This can reduce the need for traditional initiator that may be more hazardous or generate more waste.
4) **Solvent:** Nitrogen dioxide can be used as a solvent for certain reactions, such as the synthesis of some metal – organic frameworks. This can be a more environmentally friendly alternatives to traditional solvents that may be more toxic or volatile.

Nitrogen dioxide can be a useful reagent in green chemistry applications when used safely and responsibly. It is important to note that nitrogen dioxide can be hazardous to human health and environment, so proper handling and disposal procedures must be followed.

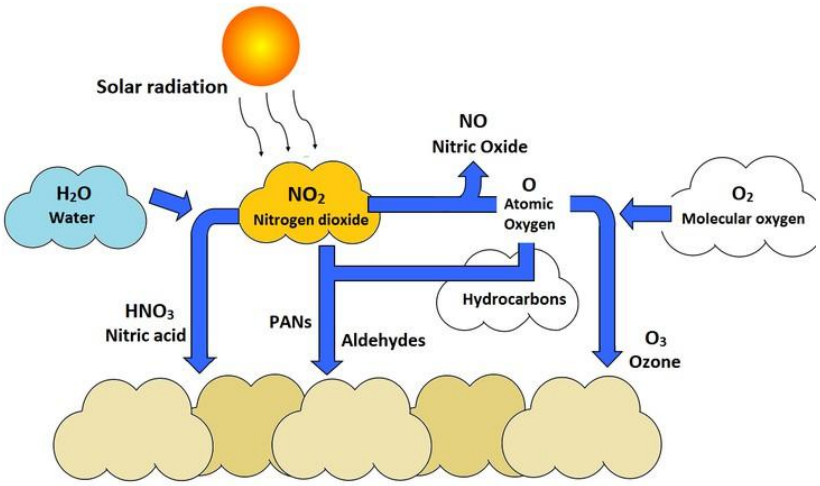
## ■ I choose $NO_2$ as my review topic because –

$NO_2$ or Nitrogen dioxide is a relevant and important topic for review for several reasons:

1) **Health impacts:** $NO_2$ is a harmful air pollutant that can cause respiratory issues such as asthma, bronchitis, and other lung diseases. It has been linked to increased hospitalizations and premature deaths, particular in urban areas with high traffic congestion. **[Ref – 1,7]**




2) **<u>Environmental impacts:</u>** $NO_2$ is also a significant contributor to environmental problems such as smog and acid rain, which can have harmful effects on ecosystems and agriculture. **[Ref – 7]**




3) **<u>Climate change:</u>** $NO_2$ is also a potent green house gas, contributing to the climate change. Understanding the relationship between $NO_2$ emissions and climate change can inform strategies to reduce greenhouse gas emissions and mitigate the impacts of climate change.

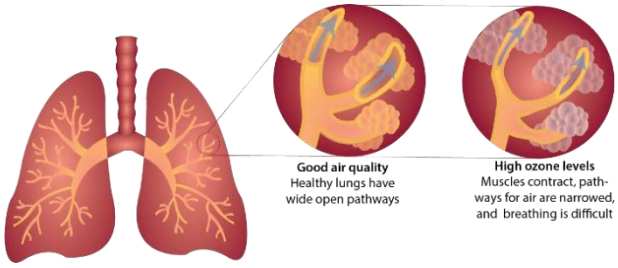
Research on $NO_2$ can help inform policy decisions and guide the development of strategies to reduce its harmful impacts. Additionally, research in this area can lead to advancements in technology and engineering, such as the development of cleaner fuels and more efficient engines.

**Nitrogen dioxide is a harmful air pollutant that can have negative effects on human health and the environment. The effects of $NO_2$ in briefly:**

## A. <u>Effects on Human Health:</u>

1) **<u>Respiratory problems:</u>** $NO_2$ can irritate the respiratory system and cause respiratory issues such as coughing, wheezing and shortness of breath. Long – term exposure

to $NO_2$ can worsen existing respiratory conditions such as asthma and bronchitis.




2) **<u>Cardiovascular problems:</u>** $NO_2$ can increase the risk of cardiovascular diseases, including heart attacks and stroke.

3) **<u>Increased risk of infections:</u>** Exposure to $NO_2$ can increase the risk of respiratory infections.

## B. <u>Effects on the Environment:</u>

1) **<u>Formation of smog:</u>** $NO_2$ can react with other pollutants in the atmosphere to form ground – level ozone, which is a major component of smog. Smog can harm plants and reduce crop yields, as well irritate the eyes, nose and throat in humans.

$$NO_{2(g)} \xrightarrow{h\nu} NO_{(g)} + O_{(g)}$$

Nitrogen dioxide — Nitric oxide

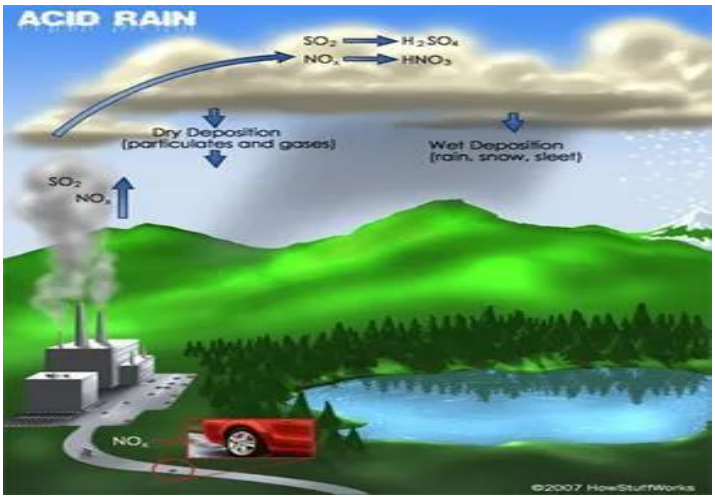
$$O_{(g)} + O_{2(g)} \longleftrightarrow O_{3(g)}$$

$$O_{3(g)} + NO_{(g)} \longrightarrow NO_{2(g)} + O_{2(g)}$$

$$3CH_4 + 2O_3 \rightarrow 3CH_2{=}O + 3H_2O$$

Formaldehyde

2) **<u>Acid Rain:</u>** $NO_2$ can contribute to the formation of acid rain, which can harm forests, lakes, and other ecosystem, as well as damage buildings and infrastructure.



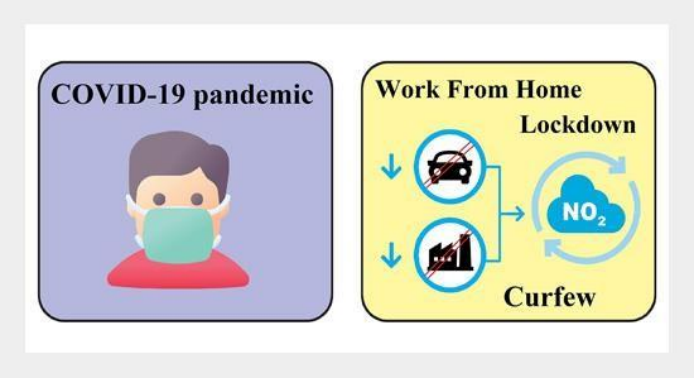

3) **<u>Climate change:</u>** $NO_2$ is a potent greenhouse gas that contributes to climate change and its associated impacts, such as rising sea level and more frequent and intense weather events.

Reducing emission of $NO_2$ is crucial for protecting both human health and the environment, and can be achieved throat policies and actions that promote cleaner energy sources, more efficient transportation, and other measures to reduce emissions from industrial and other sources.

## ■ REDUCE THE USE OF EXCESSIVE $NO_2$:

Some ways to reduce the use of excessive $NO_2$ –

1) **<u>Reduce driving:</u>** Vehicles are a major source of $NO_2$ emissions, so reducing driving or carpooling can help to reduce the amount of $NO_2$ released into the air. **[Ref- 1]**




2) **<u>Use public transportation:</u>** Public transportation emits fewer $NO_2$ emissions per person compared to individuals' cars, so using buses, trains or subways instead of driving can help to reduce $NO_2$.

3) **Use electric vehicles:** Electric vehicles emit significantly fewer $NO_2$ emissions compared to gasoline or diesel vehicles, so switching to electric vehicles can be an effective way to reduce $NO_2$.
4) **Use energy efficient appliances:** Burning fossil fuels to generate electricity also contributes to $NO_2$ emissions, so using energy – efficient appliances and devices can help to reduce the amount of $NO_2$ released into the air.
5) **Use renewable energy sources –** Using renewable energy sources like solar, wind or hydro power to generate electricity can help to reduce $NO_2$ emissions from energy production.
6) **Support government regulations:** Governments can enact regulations and standards to limit $NO_2$ emissions from various sources like vehicles or power plants, so supporting these regulations can also help to reduce $NO_2$.

Reducing the use of excessive $NO_2$ required a combination of individual actions and policy changes to reduce emissions from various sources.

## ■APPLICATIONS OF NITROGEN DIOXIDE:

It has several practical applications in various fields. Here are some common applications of $NO_2$ –

1) **Industrial processes:** $NO_2$ is commonly used in the chemical industry as a reagent and oxidizing agent in the production of nitric acid, dyes, and other chemicals.
2) **Rocket propulsion:** $NO_2$ is used as a propellant in rockets and missiles, where it is used as an oxidizer for liquid fuels.

3) **Sterilization:** $NO_2$ can be used to sterilize medical equipment, pharmaceuticals and food products. It is used in this capacity because it is strong oxidizing agent that can kill microorganisms and other pathogens.

4) **Agriculture:** $NO_2$ can be used as a fertilizer in agriculture because it is an important component of nitrogen – based fertilizer. It helps to increase crop yields and improve soil fertility.
5) **Air conditioning:** $NO_2$ is used in some air conditioning systems as a refrigerant. It has a low boiling point and can be used to cool air in refrigeration cycles.

## ■CHEMICAL PROPERTIES OF NITROGEN DIOXIDE ($NO_2$):

1) **Thermal properties:** Exists in equilibrium dinitrogen tetroxide gas.

$$2NO_2 \longleftrightarrow N_2O_4$$

2) **As an oxidizer:** Due to the weakness of the N – O bond, $NO_2$ is a strong oxidizer.
3) **Hydrolysis reaction:** Hydrolysis reaction produces nitrous acid and nitric acid.

$2NO_2\ (N_2O_4) + H_2O \longrightarrow HNO_2 + HNO_3$

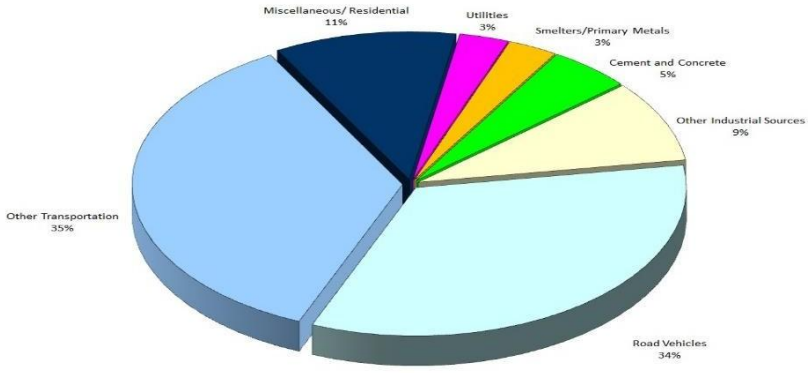
4) It is a negligibly slow reaction at all concentrations of $NO_2$.
5) **Formation of Nitrites:** Corresponding nitrites are form by alkyl and metal iodides.

$2CH_3I + 2NO_2 \longrightarrow 2CH_3NO_2 + I_2$

$TiI_4 + 4NO_2 \longrightarrow Ti\ (NO_2)_4 + 2I_2$

## ■ SOURCES OF $NO_2$ (Nitrogen dioxide):

The main source of nitrogen dioxide resulting for human activities is the combustion of fossil fuels (coal, gas and oil ) especially fuel used in cars . It is also produced from making nitric acid, welding and using explosives, refining of petrol and metals, commercial manufacturing, and food manufacturing. Some natural sources are – volcanoes, and bacteria.




## ■ FUTURE IMPACTS OF $NO_2$ (Nitrogen dioxide):

### A. Future impacts of excessive use of $NO_2$:

The excessive use of $NO_2$ can have significant negative impacts of the environment and human health in the future. there are some future impacts of excessive $NO_2$ use-

1) **Worsening air quality:** $NO_2$ is a major contribute to poor air quality, which can lead to increased respiratory problems and other negative health effects.

2) **Climate change:** $NO_2$ is a greenhouse gas that contributes to climate change, and its excessive use can exacerbate global warming and its impacts on the environment and human societies.
3) **Biodiversity loss:** Excessive $NO_2$ use can lead to acid rain, which can damage forest, waterways, and other natural habitats, leading to a loss of biodiversity.
4) **Food security:** $NO_2$ emissions can reduce crop yields and food quality, leading to a potential threat to global food security.
5) **Public health:** Excessive $NO_2$ use can have severe health impacts on humans, including respiratory problems, cardiovascular diseases and cancer.

## B. Future impacts of $NO_2$ after control the use of excessive $NO_2$:

1) **Improved air quality:** By reducing $NO_2$ emissions, air quality can be improved, leading to fewer respiratory problems and other negative health effects.

2) **Lower health risk:** With lower levels of $NO_2$ in the air, people would be less likely to experience respiratory problems, heart diseases, and stroke. This would lead to a reduction in healthcare costs and an overall improvement in public health.
3) **Reduced environmental impacts:** $NO_2$ contributes to the formation of acid rain and smog, which can harm ecosystems and damage crops. By reducing $NO_2$ emissions, we could minimize these negative impacts and help to protect the environment.
4) **Mitigated climate change:** $NO_2$ is a potent greenhouse gas that contributes to climate change. By reducing $NO_2$ emissions, we could help to mitigated the effects of climate change and reduce the risk of global warming.

Controlling the use of excessive $NO_2$ would have a significant positive impact on human health, the environment, and the planet's climate.

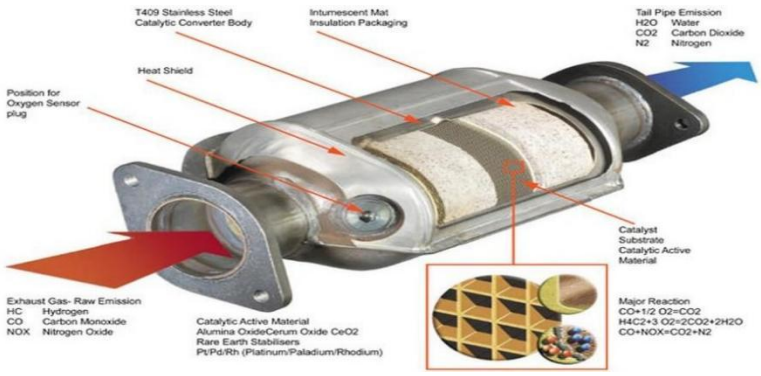
So prevent the such negative future impacts it is essential to reduce the use of excessive $NO_2$ by promoting cleaner energy sources, using sustainable transportation, implementing stricter environmental regulations. By taking proactive steps to reduce $NO_2$ use, we can protect both the environment and human health in the future.

## ■ EXPERIMENTAL RELEVANCE:

### ● APPROACH USING GREEN CHEMISTRY TO REDUCE THE HARMFUL EFFECTS OF NITROGEN DIOXIDE ($NO_2$):

Green chemistry offers various approaches to reducing the harmful effects of nitrogen dioxide (NO2) on the environment and human health. Here are some possible ways:

1) **Use catalysts:** One way to reduce NO2 emissions is to use catalysts in industrial processes that generate NO2. Catalysts are substances that speed up chemical reactions and reduce the amount of energy required. For example, catalytic converters in cars reduce NO2 emissions by converting them into less harmful gases such as nitrogen, oxygen, and water.




2) **Use renewable energy:** Another approach to reducing NO2 emissions is to shift to renewable energy sources, such as solar and wind power, which produce fewer emissions than traditional energy sources like coal or oil.

3) **<u>Improve energy efficiency</u>:** By improving energy efficiency in industrial processes, we can reduce the amount of energy needed to produce goods and services, which in turn reduces NO2 emissions. This can be achieved through various measures such as using energy-efficient equipment, optimizing processes, and reducing waste.

4) **<u>Use alternative feedstocks</u>:** In chemical manufacturing, alternative feedstocks can be used instead of traditional fossil fuel-derived feedstocks. For example, biomass-derived feedstocks, such as agricultural waste or algae, can be used as an alternative source of chemicals. This approach reduces NO2 emissions and provides a sustainable source of raw materials.

5) **<u>Recycling and waste reduction</u>:** Recycling materials reduces the need for new production, which in turn reduces NO2 emissions. Additionally, by reducing waste generation, we can reduce the amount of NO2 released during waste disposal.


These are just a few of the approaches that can be taken to reduce the harmful effects of NO2 using green chemistry. By adopting these methods and other sustainable practices, we can work towards a cleaner and healthier environment.

## ■<u>SOME TECHNIQUES TO MEASURE NITROGEN DIOXIDE:</u>

1) **Chemiluminescence** – It is a commonly used to technique for measuring nitrogen dioxide concentration in air sample. **[Ref – 8]**
2) **Differential Optical Absorption:** It is an optical technique that uses absorption of light to measure, $NO_2$ concentration in the atmosphere.
3) **A Gas Chromatography:** It is used for analyses of stack and Exhaust gases. **[Ref – 3]**

The choice of techniques for measuring and analyzed nitrogen dioxide depends on the special application and requirements of the analysis.

## ■ POLICIES GIVEN BY THE GOVERNMENT:

To address the issues of nitrogen dioxide pollution, various policies have been implemented by governments and organizations around the world. Here are some examples –

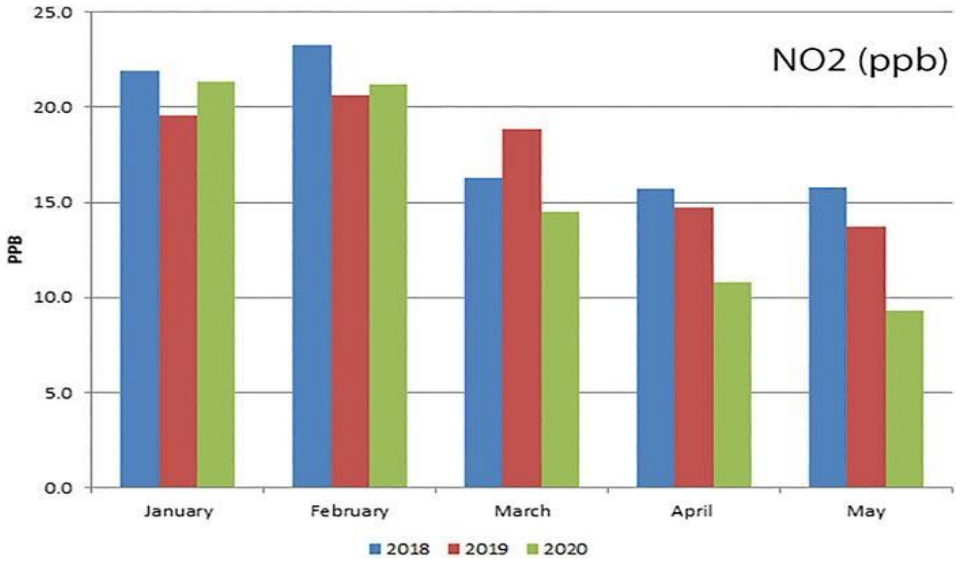
1) **Emissions Standards:** Governments have set emission standards for various industries and transportation sectors to limit the amount of nitrogen dioxide ($NO_2$) released into the atmosphere. For example, the European Union has set emission standards for cars, trucks, and buses under the Euro standards, which aim to reduce $NO_2$ emissions.
2) **Low Emission Zones:** Some cities have implemented low emission zones where vehicles with high emissions are restricted or banned. This policy encourages people to use public transportation or low – emission vehicles and reduces the amount of $NO_2$ in the air.
3) **Air Quality Monitoring:** Governments and organizations regularly monitor air quality to track $NO_2$ levels and take action when levels exceed safety standards. This can include issuing health warnings, implementing traffic restrictions, and introducing pollution – reducing measures.

## Air Quality Guide for Nitrogen Dioxide

| Air Quality Index | Protect Your Health Near Roadways |
|---|---|
| Good (0-50) | No health impacts are expected when air quality is in this range. |
| Moderate (51-100) | Individuals who are unusually sensitive to nitrogen dioxide should consider limiting prolonged outdoor exertion. |
| Unhealthy for Sensitive Groups (101-150) | The following groups should limit prolonged outdoor exertion:<br>• People with lung disease, such as asthma<br>• Children and older adults |
| Unhealthy (151-200) | The following groups should avoid prolonged outdoor exertion:<br>• People with lung disease, such as asthma<br>• Children and older adults<br>Everyone else should limit prolonged outdoor exertion. |
| Very Unhealthy (201-300) | The following groups should avoid all outdoor exertion:<br>• People with lung disease, such as asthma<br>• Children and older adults<br>Everyone else should limit outdoor exertion. |

**[Ref – 11]**

4) **Green Transport:** Encouraging the use of sustainable modes of transport such as cycling, walking, and electric vehicles can reduce $NO_2$ emissions from transportation.
5) **Industrial Regulations:** Governments may implement regulations on industries to reduce $NO_2$ emissions from industrial processes. This can include requiring the installation of pollution control equipment or reducing the use of fossil fuels.
6) **Education and Awareness:** Educating the public about the harmful effects of $NO_2$ pollution and ways to reduce exposure can encourage individuals to take action to reduce their own emissions.



These policies aim to reduce the amount of $NO_2$ in the air and improve air quality, which can have significant health and environmental benefits.

# CONCLUSION

It is a gaseous air pollutant with harmful effects on human health and the environment. It is primarily emitted by combustion processes in transportation, industry and building. Exposure to Nitrogen dioxide has been linked to respiratory problems and other negative health impacts, particularly in vulnerably populations such as children and the elderly.

To mitigate the negative impacts of Nitrogen dioxide, effects should be made to reduce its emissions through cleaner combustion technologies, use of alternative transportation modes, and other measures. Monitoring and controlling nitrogen dioxide concentration in ambient air and occupational settings are also crucial to protect public health and worker safety. Research on nitrogen dioxide is ongoing, particularly in areas such as atmospheric chemistry, health effects and material science, to better understand its impacts and develop effective solutions to reduce its emissions and exposures.

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