



## Research on the Anti-Psychotic Drug Lithium Carbonate Effective Against Bipolar Disorder

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### ABSTRACT

Bipolar disorder is classified as a chronic or episodic mental illness, meaning that it manifests sporadically and irregularly. It can result in odd, frequently drastic, and erratic shifts in mood, energy, activity level, and ability to concentrate or focus. Manic-depressive illness and manic depression are older terminology that are occasionally used to refer to bipolar disorder. While everyone experiences ups and downs on a regular basis, bipolar disorder is unique. There might be a wide spectrum of mood swings. A person experiencing a manic episode may feel extremely cheerful, agitated, or "up," and their level of activity will noticeably increase. A person experiencing a depressive episode may have very low activity levels accompanied by feelings of sadness, indifference, or hopelessness. Hypomanic episodes are similar to manic episodes in certain individuals but are less severe and bothersome. (DSM-III) is the same as Manic Depressive Illness, Manic in the previous DSM-II classification scheme. In addition, lithium is recommended as a maintenance medication for people with bipolar disorder diagnoses. Both the frequency and potential intensity of manic episodes are decreased with maintenance therapy. Mania is commonly characterized by pressure in speech, motor hyperactivity, decreased sleep needs, flight of ideas, grandiosity, euphoria, bad judgment, aggression, and maybe animosity. Lithium may cause a patient going through a manic episode to experience a return to normal symptomatology in one to three weeks.

**Keywords:** Bipolar disorder, Hypomanic, DSM-II, Grandiosity, euphoria.

### Introduction

Mental illnesses such as bipolar disorder can be classified as episodic (occurring periodically and at irregular intervals) or chronic (permanent or constantly recurrent). The more archaic phrases "manic-depressive disorder" or "manic depression" are occasionally used to describe bipolar illness.

While everyone experiences occasional highs and lows, people with bipolar illness may have extremely wide mood swings. Manic episodes, or abnormally high moods in which a person may feel extremely joyful, agitated, or "up," with a noticeable increase in activity level, are experienced by those with the disease. They may also experience depressive episodes, which are marked by extreme inactivity and feelings of melancholy, indifference, or hopelessness. Similar to manic episodes, hypomanic episodes can occur in certain persons, although they are not severe enough to need hospitalization or significantly impede social or vocational functioning.

Bipolar disorder symptoms might appear in children. Suicide, losing one's work, and functioning, and family strife can all be significantly influenced by bipolar disease. On the other hand, appropriate care can result in enhanced functionality and a higher standard of living. In the former DSM-II nomenclature, Manic Depressive Illness is similar to Manic Bipolar Disorder (DSM-III).

In addition, lithium is recommended as a maintenance medication for people with bipolar disorder diagnoses. The frequency and potential strength of manic episodes are both decreased with maintenance therapy.

Mania is commonly characterized by pressure in speech, motor hyperactivity, decreased sleep demand, grandiosity, euphoria, bad judgment, aggression, and maybe animosity. Lithium may cause a patient going through a manic episode to experience a return to normal symptomatology in one to three weeks. Since the risk of lithium toxicity is quite high in patients with major renal or cardiovascular illness, severe debilitation or dehydration, salt depletion, or diuretics, lithium should normally not be given to these individuals.

Lithium treatment may be started with extreme caution if the mental illness is life-threatening and the patient does not react to other interventions. This may involve measuring the patient's serum lithium levels every day and adjusting to the low dosages that the patient typically tolerates. In these situations, hospitalization is required.

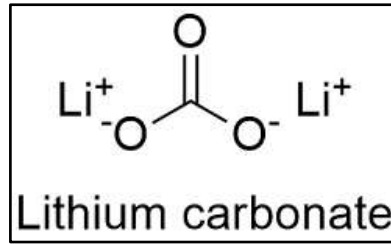


Figure 1: Structure of Lithium Carbonate

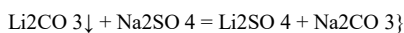
## Synthesis of Lithium Carbonate

In the earth, lithium is a light, uncommon, and restricted metal. It is a novel energy material and strategic metal that has recently found application in a number of industries, including ceramics, batteries, nuclear energy, aerospace, medicines, and the metallurgical sector [1-3]. Lithium-ion batteries have attracted a lot of attention lately as achieving a high specific capacity for electrode material depends on the multi-electron reaction of lithium. Due to its strong electrochemical inertness and use as a raw material for the synthesis of lithium conductors, lithium carbonate ( $\text{Li}_2\text{CO}_3$ ) is regarded as a suitable component for the production of the cathode's protective layer [4-6].

Elevated purity  $\text{Li}_2\text{CO}_3$  is mostly made from lithium minerals like spodumene ( $\text{Li}_2\text{O} \cdot \text{Al}_2\text{O}_3 \cdot 2\text{SiO}_2$ ), which is found in pegmatites, the second-largest source of lithium [7-9].  $\text{Li}_2\text{CO}_3$  is commonly utilized in lithium-ion batteries. The sulfuric acid method is a conventional method of extracting lithium from sources containing spodumene. It involves two primary steps: carbonation to produce lithium carbonate and leaching by sulfuric acid solutions to produce a lithium sulfate solution [10-12]. Based on the high reactivity of  $\beta$ -spodumene through calcination at  $1100^\circ\text{C}$ , sulfuric acid is mixed and roasted with concentrated sulfuric acid ( $\text{H}_2\text{SO}_4$ ) at  $250^\circ\text{C}$ . In the 20th century, a number of investigations were carried out on the extraction of lithium from spodumene; however, the procedures were abandoned because of the high temperature, long duration, and low lithium yield [7,14]. As a result, current research on the sulfuric acid process is extensive. The sulfuric acid reaction is represented by the following equation:

Adding  $\text{H}_2\text{SO}_4(l)$  to  $2\text{LiAlSi}_2\text{O}_6(s)$  yields  $2\text{HAlSi}_2\text{O}_6(s) + \text{Li}_2\text{SO}_4(s)$ .

According to the following equation, the reaction of sodium carbonate is typically what triggers the second major stage, carbonation [10,11,13, 15].



Since South Korea currently imports lithium raw materials to make lithium-ion batteries, a reliable resource supply system must be established in order for local industries to survive in the cutthroat global market.

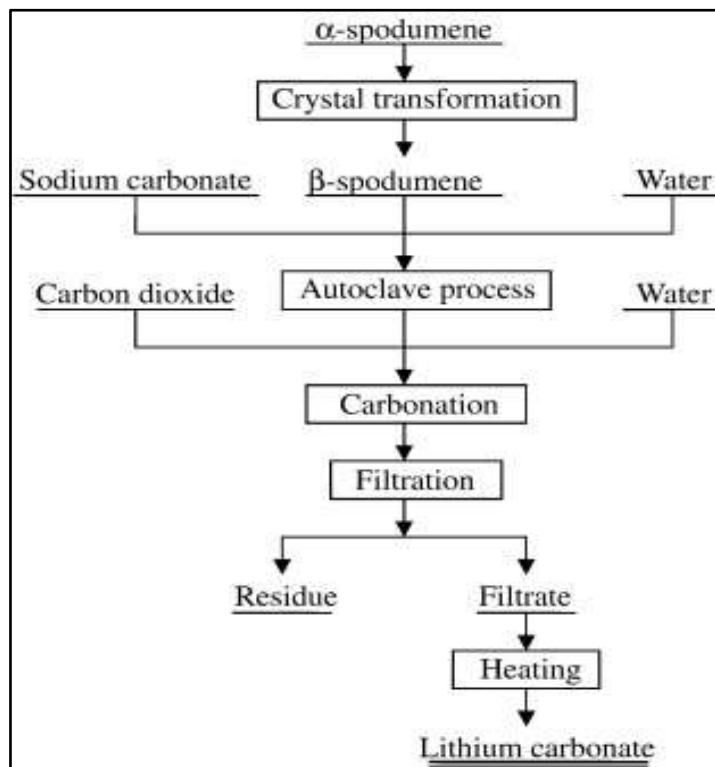


Figure 2: Synthesis method of Lithium Carbonate for bipolar disorder

## Symptoms of Bipolar Disorder

Bipolar disorder symptoms can differ. Manic, depressive, or "mixed" episodes can occur in a person with bipolar disorder. Both manic and depressed symptoms are present in a mixed episode. The effects of these mood swings can persist for a week or two. The symptoms are present every day for the majority of the day throughout an episode. Episodes of mood are strong. The emotions are strong and coincide with observable behavioral, energetic, or activity shifts in others.

SYMPTOMS OF A MANIC EPISODE	SYMPTOMS OF A DEPRESSIVE EPISODE
Feeling very up, high, elated, or extremely irritable or touchy	Feeling very down or sad, or anhedonia
Feeling jumpy or wired, more active than usual	Feeling slowed down or restless
Racing thoughts	Trouble concentrating or making decisions
Decreased need for sleep	Trouble falling asleep, waking up too early, or sleeping too much
Talking fast about a lot of different things ("flight of ideas")	Talking very slowly, feeling like you have nothing to say, or forgetting a lot
Excessive appetite for food, drinking, sex, or other pleasurable activities	Lack of interest in almost all activities
Thinking you can do a lot of things at once without getting tired	Unable to do even simple things
Feeling like you are unusually important, talented, or powerful	Feeling hopeless or worthless, or thinking about death or suicide

Figure 3: Symptoms of Bipolar Disorder.

## Types of Bipolar Disorder

There are three main forms of bipolar disorder, and they are all characterized by distinct shifts in energy, activity, and mood. These emotions range from very sad, "down," hopeless, or low activity times (depressive episodes) to periods of tremendously "up," elated, and energetic behavior or increased activity levels (manic episodes). Individuals who have bipolar illness may also experience mood swings between depression and a normal, euthymic state. "Rapid cycling" refers to manic or depressive episodes occurring four or more times in a year.

**Bipolar I Disorder** is characterized by manic episodes that continue seven days or longer (most of the day, almost every day) or by severe enough manic symptoms to require hospitalization. Separate depressed episodes also usually happen, and they usually persist for two weeks or longer. It is also possible to experience mixed-feature episodes of mood disruption, which include symptoms of both mania and depression concurrently.

**Cyclothymic Disorder** (also known as cyclothymia) is characterized by recurrent periods of hypomanic and depressed symptoms that are neither severe enough nor prolonged enough to be considered episodes.

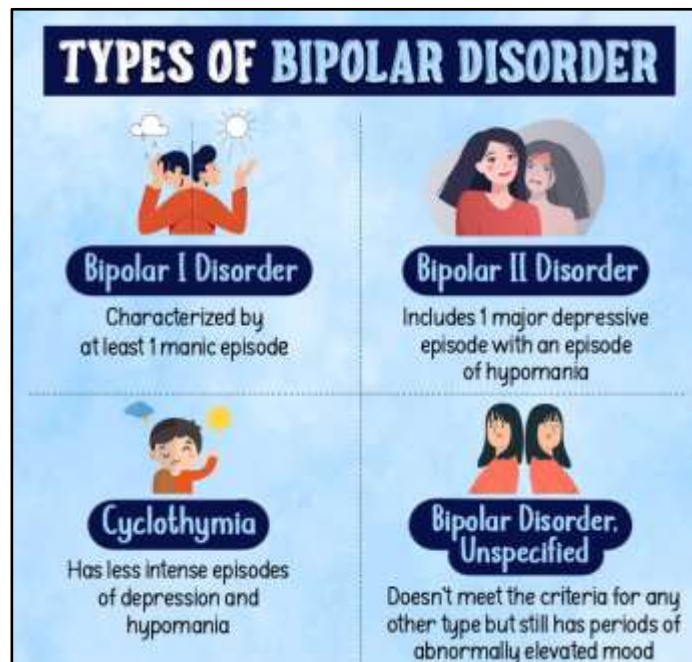


Figure 4: Types of Bipolar disorder.

## Conditions Occur With Bipolar Disorder

Many people with bipolar disorder also may have other mental health disorders or conditions such as:

**Psychosis.** Psychotic symptoms, such as hallucinations or delusions, can occasionally coexist with severe episodes of mania or depression. The individual's severe mood is often reflected in the psychotic symptoms. For instance: A person experiencing psychotic symptoms during a manic episode can think, in error, that he or she is well-known, wealthy, or endowed with extraordinary abilities. When experiencing psychotic symptoms during a depressed episode, a person may think they have committed a crime or are hopelessly broke.

**Anxiety Disorders and Attention-Deficit/Hyperactivity Disorder (ADHD).** Anxiety disorders and ADHD often are diagnosed in people with bipolar disorder.

**Misuse of Drugs or Alcohol.** People with bipolar disorder are more prone to misusing drugs or alcohol.

**Eating Disorders.** People with bipolar disorder occasionally may have an eating disorder, such as binge eating or bulimia.



Figure 5: Triggers in Bipolar Disorder

### When does bipolar disorder begin?

The initial indications of bipolar disorder are increasingly being identified in early adulthood or childhood. However, the symptoms may be less common the younger the person is when they first appear. Bipolar disorder is sometimes misdiagnosed as teenage distress or rebellion due to similar symptoms that can be confused for these issues.

Bipolar disorder can manifest during or soon after pregnancy in certain women. After pregnancy, mania, or a "high," affects only approximately one mother out of every thousand. Postpartum depression is more common. If following childbirth, you or a loved one has experienced severe depression symptoms that persist longer than two weeks, you or they should.

### What causes bipolar disorder?

Bipolar disorder is caused by multiple variables, the exact mechanism of which is unknown. Nonetheless, there is substantial evidence supporting the importance of biological elements, such as genetics. This does not imply that a person must inherit the genes; during conception, the relevant genes may change. All of the body's cells and their contents are designed according to their genes. Bipolar disease may arise from defective proteins made by brain cells as a result of genetic alterations, according to scientists. These days, scientists are examining both the genes themselves and the different proteins that may be impacted by bipolar disorder. These consist of:

- proteins that employ neurotransmitters to trigger cell action;
- proteins involved in the synthesis of neurotransmitters, or "chemical messengers" in the brain.

We do know that challenging family dynamics or excessive stress do not contribute to bipolar disorder. However, for those who already have the illness, these things may set off an episode. Furthermore, bipolar disorder is not just a result of a dopamine or serotonin imbalance. Nonetheless, neurotransmitters could be impacted as the disease flares up.

### How is bipolar disorder diagnosed?

A physician or other health care practitioner may: Conduct a thorough physical examination in order to diagnose bipolar disorder. To rule out additional ailments, order medical testing. Send the person for a psychiatrist's assessment.

Bipolar disorder is diagnosed by a psychiatrist or other mental health specialist based on the patient's history, lifetime course, and symptoms. Before receiving a diagnosis, bipolar disorder affects some people for years.

This could be the case because Bipolar disorder shares symptoms with a number of other mental illnesses. A physician may suspect that the patient suffers from an alternative illness, like schizophrenia or unipolar depression. Although family and friends may observe the symptoms, they may not be aware that they are a sign of a more serious issue. It might be challenging for medical professionals to identify bipolar disorder since people with bipolar disorder frequently have co-occurring medical disorders.



Figure 6: Diagnosis of Bipolar Disorder

### Treatments

Other therapies that some patients may find useful in controlling their bipolar symptoms include: A brain stimulation technique called electroconvulsive treatment can help patients with severe bipolar disorder symptoms. This kind of therapy is typically only taken into consideration when all other therapies, such as medication or psychotherapy, have failed to improve the patient's condition or when an immediate reaction is required, like in the event of suicide risk or catatonia (a state of unresponsiveness), for example. Frequent high-intensity physical activities, like swimming, cycling, or jogging, improve sleep quality, lower anxiety and depression, and benefit the heart and brain. Consult your physician prior to beginning a new fitness program. People with bipolar illness and their doctors can monitor and treat the condition by keeping a life chart that documents daily mood symptoms, treatments, sleep habits, and life events to overcome bipolar disorder doctor may prescribe lithium carbonate of Power 400 during the start.



Figure 7: Treatment of Bipolar Disorder

### Contraindication

Since the risk of lithium toxicity is particularly high in patients with major renal or cardiovascular disease, severe debilitation or dehydration, salt depletion, or who are taking diuretics, lithium should normally not be given to these individuals. Lithium medication may be administered with extreme

caution if the mental indication is life-threatening and the patient does not respond to other interventions. This may involve daily serum lithium readings and adjusting to the often low doses tolerated by these individuals. In some cases, hospitalization is required.

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## PRECAUTIONS

Thyroid conditions that have previously occurred do not always rule out using lithium. When hypothyroidism is present, thyroid function can be carefully monitored throughout lithium stabilization and maintenance, allowing for the modification of any thyroid parameters that change as well as the possible adjustment of lithium dosages. If hypothyroidism develops during the stabilization and maintenance of lithium, additional thyroid medication may be administered.

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## ADVERSE REACTIONS

Serum lithium concentrations and patient sensitivity to lithium are typically directly correlated with the incidence and severity of adverse events. At larger doses, they usually happen more frequently and with greater severity.

Lower than 1.5 mEq/L serum lithium concentrations may cause adverse effects. Concentrations between 1.5 and 2.5 mEq/L may cause mild to moderate unpleasant responses, whereas concentrations above 2.0 mEq/L may cause moderate to severe reactions. The first few days after starting lithium medication may also bring on momentary, moderate nausea as well as overall discomfort.

Usually, these adverse effects go away when the medication is continued or is temporarily reduced or stopped. If chronic, stopping lithium medication might be necessary. At lithium concentrations below 2.0 mEq/L, symptoms such as diarrhea, vomiting, sleepiness, muscle weakness, and loss of coordination may manifest as early indicators of lithium intoxication. Higher doses may cause ataxia, tinnitus, giddiness, blurred vision, and a considerable output of diluted urine. Above 3.0 mEq/L serum lithium concentrations might result in a complicated clinical picture involving several organ systems. During the acute therapy phase, serum lithium concentrations should not be allowed to rise above 2.0 mEq/L.

The following reactions, including those that fall inside the therapeutic range, have been documented and seem to be connected to serum lithium concentrations:

### Lithium Toxicity

Lithium levels in the serum rise with an increased probability of toxicity. Higher serum lithium concentrations (>1.5 mEq/l) are associated with a higher risk. On the other hand, at serum levels below 1.5 mEq/l, people who are sensitive to lithium may show hazardous symptoms.

When lithium levels are less than 2.0 mEq/l, symptoms such as diarrhea, vomiting, sleepiness, muscle weakness, and loss of coordination may appear early and indicate lithium toxicity. Higher doses may cause ataxia, tinnitus, giddiness, blurred vision, and a considerable output of diluted urine. Above 3.0 mEq/l serum lithium levels can result in a complicated clinical picture involving several organ systems. It is not recommended to allow serum lithium levels to rise above 2.0 mEq/l when in the acute therapy period.

When starting medication for the acute manic phase, fine hand tremor, polyuria, and minor thirst may appear. These side effects may last the whole course of treatment. The first few days after starting lithium medication may also bring on temporary, mild nausea as well as overall discomfort.

Usually, these adverse effects go away with continuing therapy or a brief decrease or stop of dosage, making them a minor inconvenience rather than a crippling illness. If persistent, stopping the dosage is advised.

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## Experimental Models

### Thermogravimetric Analysis (TGA)

To confirm that lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) may undergo a phase transition with temperature, thermogravimetric analysis (TGA) was performed. A thermogravimetric change experiment of lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) was carried out in  $\text{CO}_2$  gas (300cc/min) atmosphere at temperatures ranging from  $30^\circ\text{C}$  to  $990^\circ\text{C}$  at a temperature elevation rate of  $5^\circ\text{C}/\text{min}$ . The findings. It was verified that the weight reduced between 800 and 900 degrees Celsius. This is also the expected temperature range for the phase shift of lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) powder.

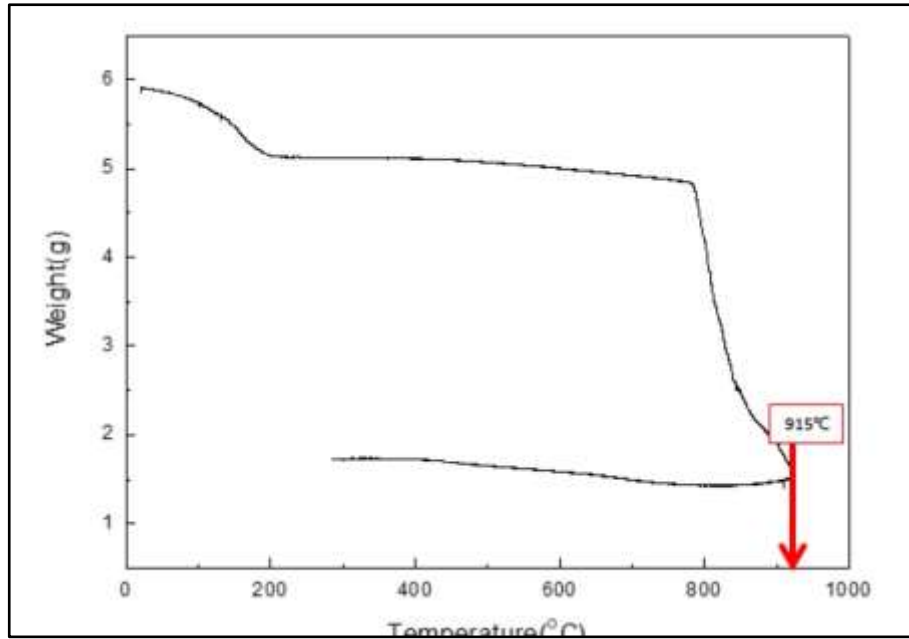


Fig. 2. TGA curve of  $\text{Li}_2\text{SO}_4$  according to various heating temperatures from 30 to 990°C under  $\text{CO}_2$  atmosphere.

#### X-ray diffraction (XRD)

Lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) and lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) reagent were employed as experimental materials in this investigation. The findings of the phase and component analyses of the study's raw materials. Phase analysis was done using X-ray diffraction (XRD), and chemical component analysis was done using energy dispersive X-ray spectroscopy (EDS) and inductively coupled plasma (ICP) analysis. The presence of the raw ingredients in the form of  $\text{Li}_2\text{SO}_4$  was verified by XRD analysis. Additionally, component analysis revealed that Li, S, and O's respective contents were 10.8wt%, 36.25wt%, and 63.75wt%.

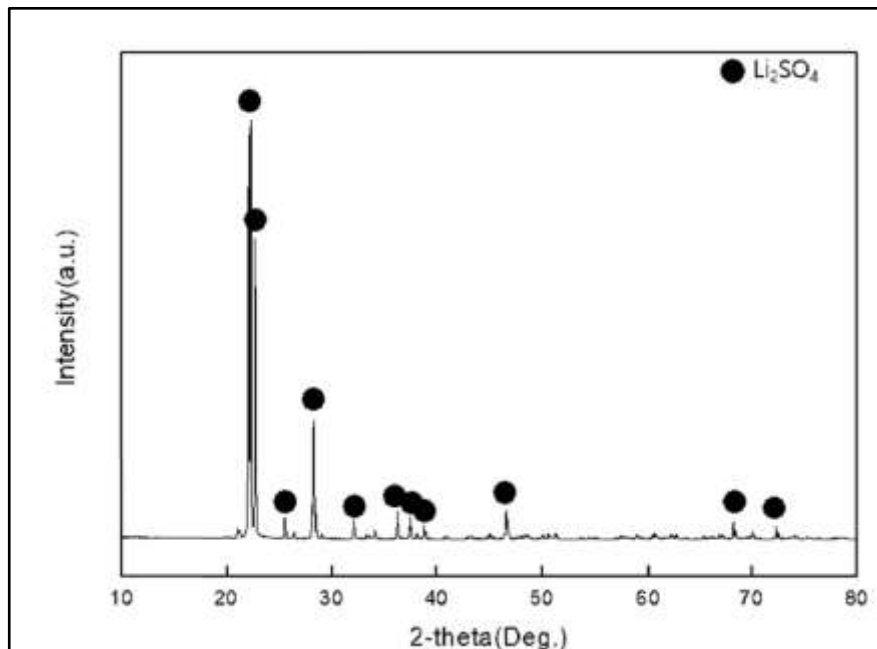
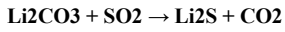
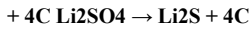


Figure 8: XRD of lithium Carbonate

## Carbonation

XRD examination was performed to demonstrate phase change following the carbonation of lithium sulfate powder. The results, broken down by temperature conditions, are displayed in Figure 4. It was determined by XRD analysis that phase change did not take place at 800°C and that phase change was complete at 900°C.

The findings of the experiment verified that 900°C was the ideal temperature for the carbonation reaction. Continuous equations can be used to conduct this reaction:



Lithium sulfate interacted with carbon first, producing lithium sulfide, according to the reactions listed. Carbon dioxide and lithium sulfide can combine to finally convert into lithium carbonate. The two reactions might occur simultaneously to fabricate lithium carbonate from lithium sulfate.

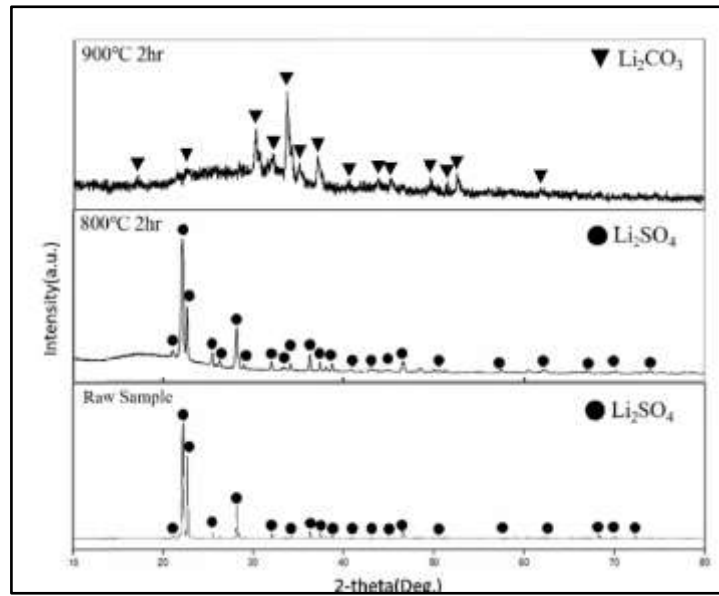


Fig. 4. XRD pattern comparison between raw sample and after carbonation at temperatures of 800°C and 900°C.

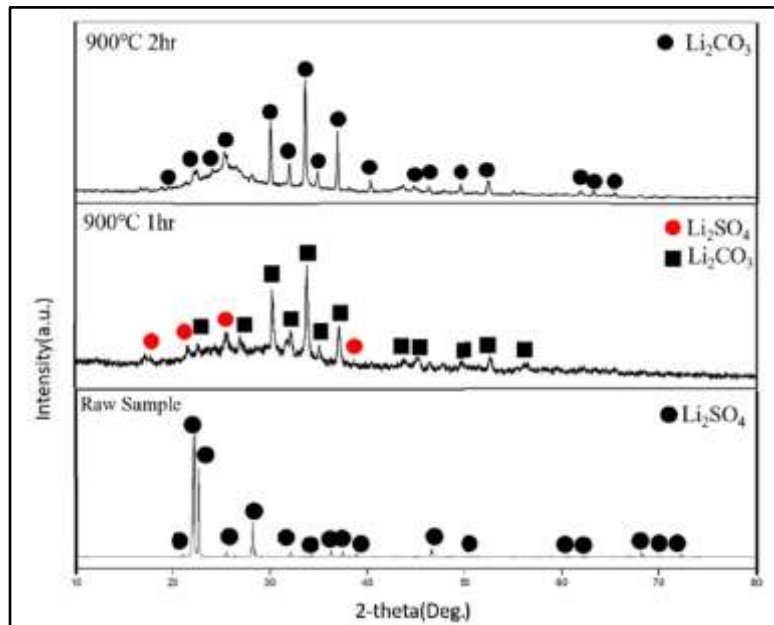


Fig. 5. XRD pattern comparison between the raw material and after carbonation for 1 and 2 hours



## Water Leaching

After lithium sulfate powder underwent phase transition, any remaining carbon powder was extracted using water leaching. Li was separated from carbon powder by using the properties that the Li phase is soluble in water and the carbon powder is insoluble in water. As can be seen in the table below, carbon powder is insoluble in water and solubility rises with decreasing water temperature in the Li phase  $\text{Li}_2\text{CO}_3$ . Since the reaction of  $\text{Li}_2\text{CO}_3$  solution in water is exothermic, it is concluded that the solubility of  $\text{Li}_2\text{CO}_3$  increases as the temperature drops. Water leaching in low-temperature water is therefore seen to be beneficial. The following parameters were used in the studies on water leaching: ratios of 1:10, 1:20, and 1:30 between powder and distilled water at room temperature; and times for the water to leach: one, two, and three hours.

Materials	$\text{Li}_2\text{CO}_3$	Carbon Powder
Solubility in Water	1.54 g/100 mL (0°C) 1.32 g/100 mL (20°C) 1.00 g/100 mL (60°C) 0.72 g/100 mL (100°C)	Insoluble

Table 1: Water Leaching

## Conclusions

In order to produce lithium carbonate using dry thermal reaction as opposed to wet thermal reaction, the goal of this study was to concentrate and recover lithium carbonate from lithium sulfate through carbonation.

1. A 1:1 ratio of lithium sulfate to additive carbon powder, a reaction temperature of 900°C, and a three-hour reaction period were the ideal parameters for the phase transition of lithium sulfate ( $\text{Li}_2\text{SO}_4$ ) through carbonation.
2. A 1:30 ratio of powder to distilled water and a 3-hour leaching period were the ideal parameters for water leaching following carbonation.
3. A lithium carbonate solution with a recovery rate of 94.53% and a lithium concentration of 10.21 wt% was obtained from the lithium solution that was ultimately recovered through carbonation and water leaching.

## Reference

- [1] Yanhcjeng Lu, Yang Liu and etc., *Ind. Eng. Chem. Res.* **53**, 11015- 11020 (2014).
- [2] J.M. Park, J.W. Jeon, M. G. Lee, *J. Korean. Sos. Mar. Environ.* **5**, 2524-2527 (2014).
- [3] Shiqiang Wang, Xunian Han and etc., *J. Chem. Eng. Data.* **61**, 1155-1161 (2016).
- [4] Yujing Bi, Tao Wang and etc., *RSC Adv.* **6**, 19233-19237 (2016).
- [5] Na Tian, Chunxiu Hua and etc., *J. Mater. Chem. A.* **3**, 14173-14177 (2015).
- [6] Yu Qiao, Jin Yi and etc., *Energy. Environ. Sci.* **11**, 1211-1217 (2018).
- [7] Colin Dessemnod, Francis Lajoie-Leroux and etc., *Metals.* **9**, 334 (2019).
- [8] A. Suharyanto, L.H. Lalasari and etc., *Mater. Sci. Eng.* **541**, 012044 (2019).
- [9] Hui Guo, Ge Kuang and etc., *Metals.* **205** (7), 1-16 (2017).
- [10] V.I. Samoilov, N.A. Kulenova, *Theor. Found. Chem. Eng.* **42** (5), 714-717. (2008).
- [11] P. G. Aguilar, T. A. Graber, *Ind. Eng. Chem. Res.* **57**, 4815-4823 (2018).
- [12] J. Jandova, P. Dvorak and etc., *J. Ceram. Silik.* **56** (1), 50-54 (2012).
- [13] L.T. Peiro, G.V. Mendez and etc., *JOM.* **65** (8), 986-996 (2013).
- [14] Wei Sheng Chen, Hsing Jung Ho, *Metals.* **321** (8), 1-16 (2018).
- [15] Wei Cai, Ruosong Chen and etc., *Crystals.* **8** (19), 1-8 (2018).
- [16] N. Ding, X.W. Ge, C.H. Chen. *Mater. Res. Bull.* **40**, 1451-1459 (2005).
- [17] M.K. Jeong, C.S. Hwang, C.S. Choi, *Clean. Tech.* **12** (2), 101-106 (2006).
- [18] J. Khanderi, J.J. Schneider, *Eur. J. Inorg. Chem.* **29**, 4591-4594 (2010).

[19] J.H. Moon, J.E. Ahn, and etc., *Applied Chemistry* **16** (1), 73-79 (2012).

[10] S.M. Shin, D.J. Shin, J.P. Wang, *Arch. Metall. Mater.* **64**, 2, 481-485 (2019).

[21] H.J. Ahn, J.W. Ahn and etc., *J. Korean Inst. Resour. Recyc.* **23**, 21-27 (2014).

[22] J.W. Ahn, H.J. Ahn, S.H. Son and etc., *J. Korean Inst. Resour.*