

Dual modification of acid hydrolysis and annealing on resistant starch: a systematic review and meta-optimization

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Abstract

Resistant starch (RS) has potentials for the development of functional food. Dual modification techniques, i.e., acid hydrolysis (AH) and annealing (ANN), were applied to raise RS content. However, several individual studies yielded varying results. Some reported that these techniques could increase the quantity of RS, while others reported otherwise. This discrepancy has not been explained, remaining an intriguing space for discussion. Therefore, this current work aimed to determine the effects of dual modification methods on resistant starch content through systematic review and meta-optimization approach. The study was conducted in 3 stages i.e., systematic review (SR), meta-analysis (MA), and response surface methodology (RSM). Data analysis for SR was based on PRISMA guidelines. The main output of MA was the effect size in standardized mean difference (SMD) values, calculated using the Hedge's method for random-effects models. RSM was used to optimize the result of MA using 3D surface chart. The main result of SR showed 62.5% of the data points decreased RS content, which follows MA result that AH and ANN decreased RS very significantly ($p < 0.001$; SMD: -10.608; 95% CI: -13.704 to -7.511). Meta-optimization using RSM was also showing a decrease in RS (parameter at 6 hrs of acid hydrolysis and 50°C of annealing incubation temperature, showed the smallest decreased). This research concluded that dual modification of AH and ANN still require broadly more experimental research data in order that it can be adequate to discover the optimum parameters to increase the RS.

1. Introduction

Starches from different botanical sources such as wheat, potato, rice, maize, and other tropical plants are the main carbohydrate in human nutrition and offer a wide range of properties to achieve desired food product qualities (Chen *et al.*, 2018). Chemically, starch constitutes a carbohydrate polymer that is composed of α -D-glucose units linked by α -1,4 and α -1,6 bonds, which form the nearly linear amylose (AM) and highly branched amylopectin (AP). Because of its properties, starch, either native or modified form can be applied in numerous industries, including sweeteners (Waterschoot *et al.*, 2014).

Resistant starch (RS) is described as the aggregate of starch and its breakdown products that do not get absorbed in the small intestine of healthy individuals. Interest in RS has seen a substantial surge over the past twenty years, primarily because of its ability to generate a significant quantity of butyrate throughout the entire colon (Champ *et al.*, 2003). Currently, with the rise of starch technology, resistant starch comes with its dual functions, including triggering health benefit and improving sensory acceptance of certain food products (Rozali *et al.*, 2018). Resistant starch potentially exerts physiological benefits on colon health and shows unique functional properties, enabling to produce high quality food products, and the properties are not found in the application of traditional dietary fiber (Fuentes-Zaragoza

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et al., 2010). Research revealed that the presence of resistant starch triggered interest of some researchers to develop resistant starch. Modifying starch either physically, chemically, enzymatically or a combination of two, or several of these processes can increase the amount of resistant starch (Ashwar *et al.*, 2015).

The structure and functionality of starch chemically modified by acid hydrolysis (AH) changed markedly, but the method unaltered the granular morphology of starch (Wang and Copeland, 2015). Principally, acid hydrolysis involved the attraction of H_3O^+ molecules, allowing them to attach the oxygen atom at the α -1,4-glycosidic bonds. Furthermore, acid modification could disbranch amylopectin molecules which prompt to increase the amount of linear components in the treated starch, producing the amylose-like behavior (Kramer, 2009). The acid-hydrolysed treatment in high amylose corn starch (HAC) class 5 and class 7 resulted in the significant rise of RS content from 40.5% to 69.3% within 16 hrs (Nagahata *et al.*, 2013).

In addition, physical modification of starch can be carried out by annealing (ANN). It exposes starch to a high (>65% w/w) or moderate (40-55% w/w) level of water below the gelatinization temperature for certain period of time (Hoover and Vasanthan, 1994). Annealing treatment induces the swelling of starch granules and the release of amylose molecules moving to the continuous phase; and this remarkably changes the architecture of starch granules (de la Rosa-Millán, 2017). This method is designed to modify a glass transition temperature, leading to the rising mobility of the molecules unaccompanied by gelatinization (Neelam *et al.*, 2012). As a result, annealing procedure enables to rise RS content, which can be acquired at 80% moisture content, 24 hrs incubation time and 50-54°C incubation temperature (Faridah *et al.*, 2021).

A systematic review answers a specific research question by combining all empirical research finding which conforms to the pre-specified criteria of eligibility. The main principle of this review is the use of explicit and systematic methods that are meaningful to diminish bias; hence, it can produce a higher reliability of research findings, allowing to compose clear conclusions and decisions (Antman *et al.*, 1992; Oxman and Guyat, 1993). Meanwhile, meta-analysis statistically assesses multiple findings from former studies. In this case, the statistical procedures can be applied to any set of data, while the synthesis can be worthwhile when the collection of studies is carried out systematically (Borenstein *et al.*, 2009). Regarding response surface methodology (RSM), it is an experimental strategy aiming to examine the process space or independent variables, empirical statistical modelling to develop a

precise approximate relationship between outcome (resistant starch) and process variables (acid hydrolysis and annealing treatment), and optimization methods to find the value of the process variable that produces the desired response value (Carley *et al.*, 2004).

However, to the best of our knowledge, studies to effect on the resistant starch after dual modification of AH and ANN are rare. Therefore, this present work focuses on the use of dual starch modification, i.e., acid hydrolysis (AH) and annealing (ANN) on the resistant starch (RS), assessed by using systematic review and meta-optimization approach.

2. Materials and methods

This research was conducted in 3 stages i.e., systematic review (SR), meta-analysis (MA), and response surface methodology (RSM). This research was held in IPB University Library in November 2021–June 2022.

2.1 Protocol

Criteria for identification, screening, selection, and inclusion of cites were performed in accordance with the guideline of PRISMA (Preferred Reporting Items for Systematic reviews and Meta-analysis), while statements relevant for a literature search of dual modification of acid hydrolysis and annealing on resistant starch were reported (Moher *et al.*, 2009).

2.2 Eligibility criteria

The criteria include original studies providing the empirical results of researches discussing the relationship between acid hydrolysis and annealing on resistant starch. Inclusion criteria consisted of: (1) experimental studies examining the resistant starch; (2) consider all published; (3) studies should be in English; (4) publication year between 1990 to 2021; and (5) complete data of experiment and control. Meanwhile, exclusion criteria consisted of: (1) studies not performed dual modification; (2) information collected from comments, book, case reports, opinion letters, and editorials; (3) studies lack of primary data and/or explicit method description; and (4) systematic reviews and meta-analysis, following manual search for their references lists, ensuring that our review covered all relevant studies

2.3 Literature search

Systematic search included seven electronic databases from 1 January 1990 to 31 December 2021 i.e., PubMed, Science Direct, Wiley Online Library, ACS Publication, Springer, Semantic Scholar, and ProQuest.

The databases were searched from inception, limited to the English. The search followed these procedures: Subject Heading terms, text keywords and Boolean operators, as follows: (1) modification; (2) acid hydrolysis; (3) annealing OR ANN; (4) heat treatment; (5) resistant starch; (6) digestibility.

2.4 Study screening

The records were saved in Mendeley Reference Manager, and the duplicates were removed. After removal, the records were screened by inspecting articles' title and abstract. Afterwards, the full-text article concerning the criteria of inclusion and exclusion without considering the results were examined. Then, they were assessed based on potential inclusion independently.

2.5 Data extraction and management

Information containing the descriptive and quantitative characteristics of studies was tabulated in Microsoft Excel, covering publication details (name of researchers, year of publication, country), characteristics of study (type of analysis method, sample types, RS content, number of replications, findings), acid hydrolysis (type of acid, acid concentration, time, and temperature) and annealing (moisture content, incubation temperature, and time). Subsequently, the selection and categorization of data were performed, and data were recorded as "qualified" when they originated from researches using a completely randomized design analyzing the effect of acid hydrolysis and annealing on resistant starch content.

2.6 Result presentation and synthesis

The synthesis of qualitative and quantitative results was presented in tables and figures format. They presented the study findings on the impacts of dual modification (acid hydrolysis and annealing) to the content of resistant starch. Relationship between different types and sources of carbohydrate, methods and experimental outcomes, as well as synthesis of results were expressed in text.

2.7 Bias risk in systematic review

Checklist can be mainly a tool, as used by Cochrane reviews. The Cochrane Collaboration's methods groups introduced a new approach for assessing the quality of randomized trials. The tool includes topics such as sequence generation, allocation sequence concealment, blinding, incomplete outcome data, and selective outcome reporting (Altman *et al.*, 2008).

2.8 Meta-analysis

In this work, openMEE tool was applied in meta-analysis (Afandi *et al.*, 2021). Effect size approach used SMD (standard mean difference) Hedge's *d*, which compared the mean difference of resistant starch content between the two groups of treatments, i.e., native starch and dual modified starch. The meta-output analysis was presented as forest plot, which informed the effect size and confidence interval of each study. In this case, the effect size demonstrated the effect of treatments (acid hydrolysis and annealing) on the quantity of resistant starch, and comparison between confidence interval and null value was made to obtain the treatment effect's significance.

In the meta-analysis study, a complementary test can be carried out in the form of publication bias to measure the validity of the study (Fagerland, 2015). Calculate the fail-safe number using the method of Rosenthal is used. If the value of $N_{ft} > 5N + 10$ then publication bias is minimal (Fragkos *et al.*, 2014).

2.9 Response surface methodology

The use of RSM enables to develop, improve, and optimize processes, by using a combination of statistical and mathematical approaches (Raymond *et al.*, 2009). In this work, the model needs statistical experimental design fundamentals, regression modelling techniques, and optimization methods, in which all of these three approaches were covered in RSM (Carley *et al.*, 2004). Using RSM, optimum factor needed to produce the best result can be determined (Raymond *et al.*, 2009). RSM was conducted using Design Expert Version 12 tools. 3D surface graph was used to describe the relationship between dual modification of acid hydrolysis and annealing on resistant starch.

3. Results and discussion

3.1 Study selection and risk of bias assessment in systematic review

Figure 1 demonstrates PRISMA flow chart. The search for studies in the electronic databases successfully identified 4734 articles. Of these, 691 duplicates were removed, and 4012 studies were eliminated due to inappropriate publication year, article type, unrelated title, unrelated sample and method, study population, or outcomes of interest. Furthermore, 31 full-text articles were reviewed from the initial search, and 22 articles were rejected due to a lack of essential data in abstract and 5 articles were excluded considering incomplete data. Therefore, 4 articles published from January 1990 to December 2021 from 4 different countries conformed to inclusion criteria and were included in systematic

review. Of these 4 articles, 3 articles were excluded since they used different types and concentration of acid. From this, we performed meta-analysis and response surface methodology (RSM) process using 1 article with 9 data points.

According to the Cochrane Collaboration tool, 3 articles were categorized as being at low risk of bias, and 1 article was categorized as being some concern risk of bias. Details about risk of bias are supplied in Figure 2 and 3.

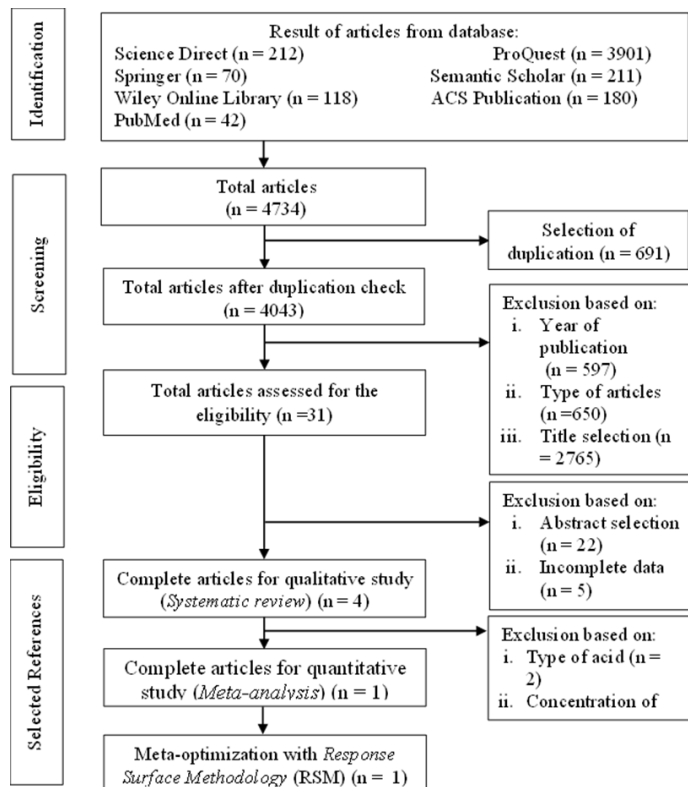


Figure 1. PRISMA flowchart describing publication selection stages.

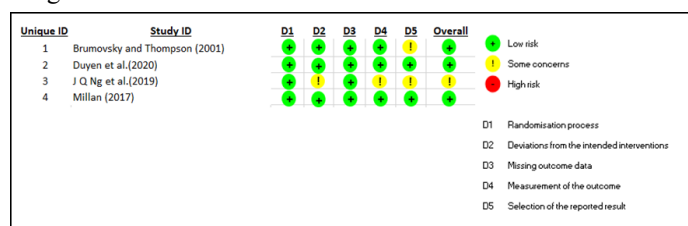


Figure 2. The result of risk of bias assessment: each risk of bias item for the included studies (green means low risk of bias, yellow means some concerns risk of bias, red means high risk of bias).

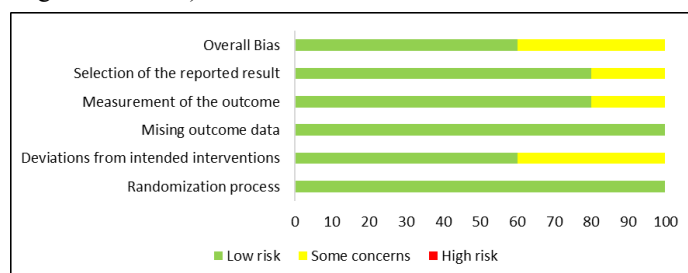


Figure 3. The result of bias assessment: each risk of bias item is shown as percentages across included studies.

3.2 Characteristics of studies

This research also follows PICO (populations, interventions, comparisons, outcomes) principle. Populations were modified starches. Interventions were starches treated by dual modification of acid hydrolysis and annealing. Comparisons were native starches. Outcomes were resistant starch.

Several samples were investigated, including maize starch, mung bean starch, sago starch, rice starch and potato starch. Among these starches, maize starch seemed to be the most popular, with amylose containing one α -(1 \rightarrow 6) glycosidic branch in each 300 D-glucose residues (Misaki and Smith, 1967). The production of resistant starch often used a high-amylose maize starch, since the digestive system of human digested it at very slow rate (Zavareze and Dias, 2011). Considering carbohydrate sources, cereals ranked as the first. Starches from cereals and tubers differ, especially resulting from internal granular architecture and size. With the greater surface of maize starch, reaction by acid and alkali treatment underwent more intensively, promoting the diffusion of chemicals into the center of starch granules. The more intensive diffusion occurred at presence of thermal treatments, enabling to unfasten relatively tightly packed molecules; thereby increasing the rate of hydrolysis (Gayin *et al.* 2016).

From the modification process, all research conducted acid hydrolysis first then followed by annealing described in Table 1. Hydrolysis is a reaction between reactants and water so that the compound decomposes. Starches with a larger shift in onset gelatinization temperature also displayed a greater percent hydrolysis. Acid hydrolysis also alters the structure of native starch, namely the molecular mass, X-ray diffraction pattern and crystallinity, susceptibility to annealing, gelatinization transition temperature, and the content of double helices (Hoover, 2000).

Typically, chemical modification is prepared before starch phase, which allows to modify specific physical properties suitable for numerous industrial applications. Chemical modification of starch obviously changed its functional properties compared to its native (Adebowale and Lawal, 2003). Meanwhile, in case of annealing treatment, although the condition of granule is maintained, substantial changes in physicochemical properties may occur, including crystallinity, gelatinization, swelling factor, solubility, viscosity and hydrolysis rate. In addition to heating time, temperature and moisture, starch source is also substantial factor contributing to the annealing properties (Yao *et al.*, 2018).

Table 1. Studies included in systematic review

References/ Country(ies)	Study	Carbohydrate Source	Type of Carbohydrates	Dual Modification Process	Findings
Brumovsky and Thompson (2001)/ USA	1	High Amylose Maize Starch	Cereals	Acid Hydrolysis continued by Annealing (AH-ANN)	After partial acid hydrolysis, annealing led to decreased gelatinization enthalpy. Annealing alone increased boiling-stable of resistant starch but decreased total of resistant starch.
Duyen et al. (2020)/Vietnam	2	Low-Amylose Mung Bean Starch Medium-Amylose Mung Bean Starch High-Amylose Mung Bean Starch			The content of resistant starch (RS) modified with citric acid-annealing was higher than that modified with citric acid-HMT or native starch in the same variety.
Ng et al. (2019)/ Malaysia	3	Sago Starch	Tubers		Combined modification of Hydrochloric Acid-Methanol-Annealing had more pronounced effect in increasing the resistant starch (RS) content and lowering the glycemic
Millan (2017)/ Mexico	4	Rice Starch Maize Starch Potato Starch	Cereals Tubers		The incubation of starches with annealing under acid conditions increased the SDS Fraction and resistant starch content.

Another research showed different result that the meta-analysis of subgroups showed that annealing led to an increase in resistant starch content across all crop groups. However, a significant increase was only observed in the cereal group. The meta-analysis of subgroups revealed that annealing increased the content of resistant starch in all crop group. However, significant increase was observed only on cereal group paraphrase (Faridah et al., 2022).

3.3 Change of resistant starch after dual modification of acid hydrolysis and annealing

All studies reported changes in resistant starch (n = 4) after introduced by dual modification of AH and ANN. Three studies (n = 3) (de la Rosa-Millán, 2017; Ng et al., 2019; Duyen et al., 2020) reported that resistant starch increased, while one study (n = 1) conducted by Brumovsky and Thompson (2001) reported the decline in resistant starch. Detailed characteristics of eligible studies are presented in Table 1.

Change of resistant starch content from research articles selected for systematic review is shown in Table 2. From the total of data points (n = 16), the result showed that dual modification of AH and ANN decreased resistant starch to 62.5% (n = 10). The decline of RS content can be associated with different parameters, i.e. starch sources, temperature and time of annealing, moisture content, types of acid used, concentration of acid and acid hydrolysis time.

Starch that is rich in amylose swells more slowly than the starch rich in amylopectin, and exhibits a loss of order within the granule, followed by its destruction (Colonna and Mercier, 1985). Maize starch is the most common sample used as source of starch due to its availability (easy to find) and cheap. As resistant starch is usually incorporated in food for health, it is tasteless and odorless; thus, it provides no undesirable effects on the sensory characteristics of the final product. This is the main reason why researchers are more interested in finding out on maize starch as a mean to develop their usage in food industry. Furthermore, potato starch may have differences. Its granular area is larger, meaning that structural rearrangement occurred more likely due to thermal treatments (Jacobs and Delcour, 1998). With the greater size of potato starch granule, the contact area tended to decline, enabling to reduce the granule collapse induced by the treatments, even considering their more relaxed internal molecular organization (Wang et al., 2016)

Temperature and time of annealing represents incubation condition, which also dictate the result of starch modification. Gomes et al. (2004) reported that temperature can affect the ability of water to penetrate into starch granules. Meanwhile time of incubation can provide a grace period against water to affect the amorphous group on starch. In addition, moisture content also affects the performance of starch modification. With the high moisture content, the hydrogen bonds were more easily disrupted, considering it was pre-treated with acid hydrolysis. Additionally, the remaining stable bonds

Table 2. Dual modification of acid hydrolysis and annealing on the change of RS in systematic review

No	References	Country (ies)	Carbohydrate source	Type of Acid	Acid Hydrolysis Treatment			Annealing Treatment			RS Level (%)					
					CA (M)	tAH (h)	TAH (°C)	MC (%)	tAnn (h)	TAnn (°C)	X ^N (%)	SD ^N	Native Starch (Control)	AH-ANN Starch	Change of RS	
1					0.3	6	25	70	24	50	78.7	0.7	74	1	6.35	RS↓
2					0.3	6	25	70	24	60	78.7	0.7	64.8	1.9	21.45	RS↓
3					0.3	6	25	70	24	70	78.7	0.7	46.6	2.1	68.88	RS↓
4	Brunovsky and Thompson (2001)	USA	High amylose maize starch	Hydrochloric acid	0.3	30	25	70	24	50	78.7	0.7	72.5	0.8	8.55	RS↓
5					0.3	30	25	70	24	60	78.7	0.7	65	1.6	21.08	RS↓
6					0.3	30	25	70	24	70	78.7	0.7	47	2.6	67.45	RS↓
7					0.3	78	25	70	24	50	78.7	0.7	72.6	1.1	8.40	RS↓
8					0.3	78	25	70	24	60	78.7	0.7	64	0.9	22.97	RS↓
9					0.3	78	25	70	24	70	78.7	0.7	42.8	1.8	83.88	RS↓
10			Low-amylose mung bean starch		0.2	24	45	70	24	45	10.1	0.7	27.1	1	62.73	RS↑
11	Duyen et al. (2020)	Vietnam	Medium-amylose mung bean starch	Citric acid	0.2	24	45	70	24	45	13.4	0.7	37.7	1.4	64.46	RS↑
12			High-amylose mung bean starch		0.2	24	45	70	24	45	15.6	0.9	41.1	1	62.04	RS↑
13	Ng et al. (2019)	Malaysia	Sago starch	Hydrochloric acid-Methanol	0.1	24	35	70	72	10	61.9	1.4	61.2	2.6	1.14	RS↓
14			Rice starch		2	4	25	90	12	55	3.26	0.83	7.77	0.1	58.04	RS↑
15	Millan (2017)	Mexico	Maize starch	Hydrochloric acid	2	4	25	90	12	55	4.36	0.47	9.67	0.53	54.91	RS↑
16			Potato starch		2	4	25	90	12	45	2.65	0.26	11.36	0.56	76.67	RS↑

CA: Concentration of acid, tAH: Time of acid hydrolysis, MC: Moisture content of annealing, tAnn: Incubation time, TAnn: Incubation temperature, X^N: Mean in Native starch, SD^N: Standard deviation in native starch, X^A: Mean in Acid hydrolysis-annealing starch, SD^A: Standard deviation in Acid Hydrolysis-annealing starch, RS: Resistant starch.

were altered by the effect of annealing. Moisture content and incubation time were deemed two essential factors contributing to the formation of SDS or RS (Jacobs and Delcour 1998; Zhou *et al.* 2014; Ashwar *et al.*, 2015). The incubation of starches with annealing under acid conditions increased the slowly digestible starch (SDS) fraction (de la Rosa-Millán, 2017). Starches with higher SDS and RS are known to confer health benefits such as preventing diabetes, cardiovascular disease and colon cancer (Shi *et al.*, 2021).

The hydrolysis process will be faster if the concentration of acid used is higher. The greater the concentration of acid used can also result in the binding of ions such as SiO₂, phosphate and salts such as Ca, Mg, Na and K contained in starch. This can cause the breakdown of monomers in starch to take place completely (Safitri, 2015).

Regarding the types of acid, a stronger acid such as HCl would induce more complete reaction of hydrolysis as it has a stronger ability to break the weak as well as the strong region of hydrogen bond possess by the polymers, thus will be much more efficient. Moreover, hydrolysis time is also influential. The same effect occurred when hydrolysis time was increased. A study reported by Chen *et al.* (2017) found that the internal cavities of starch increases when hydrolysis time is longer. This suggests that the longer the starch is in contact with acid, glycosidic bonds that are degraded is even more in number. Dual modification of AH and ANN method overall decrease greatly the amount of resistant starch.

This result is in agreement with the research of several researchers (Thompson, 2000; Chen *et al.*, 2009; Zhou *et al.*, 2016) that reported another widely used method to promote changes in starch molecules is incubation under acidic pH conditions, which results in the depolymerization of both amylose and amylopectin fractions.

3.4 Primary outcome of meta-analysis dual modification of acid hydrolysis and annealing on resistant starch

The primary outcome was the resistant starch content in forest plots (Figures 4, 5 and 6). Nine data points could be extracted from Brumovsky and Thompson (2001) due to its complete data for further optimization analysis in this research using response surface methodology (RSM). Data point is an individual unique data combination comprising sample type, carbohydrate source, acid hydrolysis parameters (acid concentration, time of acid hydrolysis, and temperature), and annealing parameters (moisture content, incubation time and temperature). These data points allowed the parameter of

time of acid hydrolysis and annealing incubation temperature to be used as variables.

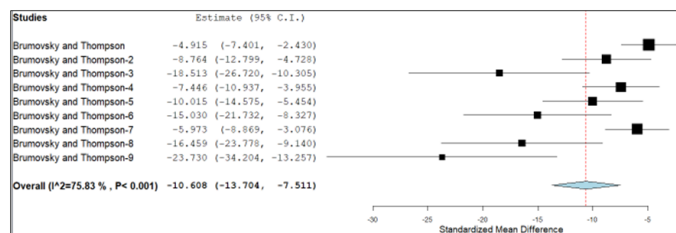


Figure 4. Forest plot overall analysis of dual modification of acid hydrolysis and annealing on resistant starch content. Negative SMD value shows the decreasing of resistant starch content.

The results of the study in the main analysis showed that dual modification of acid hydrolysis and annealing decrease resistant starch very significantly ($p < 0.001$), standardized mean difference (SMD): -10.608, confidence interval (95% CI): -13.704 to -7.511, heterogeneity (I^2): 75.83% as presented in Figure 4. This result was categorized as high heterogeneity because the value of I^2 in the parameter is more than 75%.

Subgroup analysis was done and showed that overall value of effect size for time of acid hydrolysis presented in Figure 5 and annealing incubation temperature presented in Figure 6 have the same value, also decrease the resistant starch (p -value: 0.000; SMD: -10.608; CI: -13.704 to -7.511).

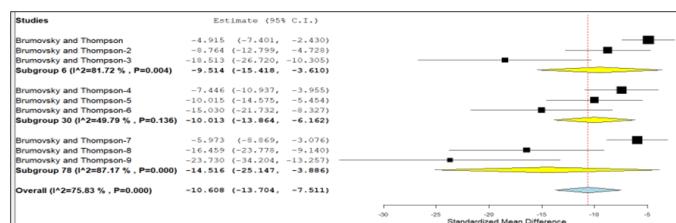


Figure 5. Forest plot of time of acid hydrolysis sub-group meta-analysis. Negative SMD value shows the decreasing of resistant starch content.

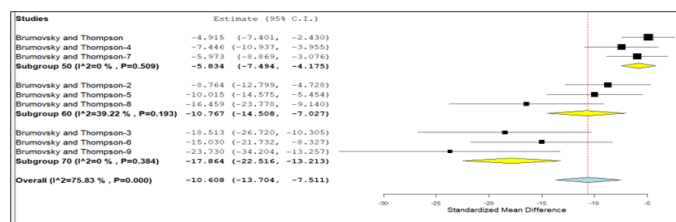


Figure 6. Forest plot of annealing incubation temperature sub-group meta-analysis. Negative SMD value shows the decreasing of resistant starch content.

The parameter of acid hydrolysis showed the levels of resistant starch with the smallest decrease, namely the sub-group time of acid hydrolysis at 6 hrs (p -value: 0.04; SMD: -9.514; CI: -15.418 to -3.610) presented in Figure 5 and annealing incubation temperature of 50°C

presented in Figure 6 (*p*-value: 0.509; SMD: -5.834; CI: -7.494 to -4.175).

There are several types of acids that could be used for acid hydrolysis such as hydrochloric acid, sulfuric acid, trifluoroacetic acid, formic acid and nitric acid. Most of the scientific studies found above use hydrochloric acids as hydrolysing reagent. Chen (2015) reported that there were previous studies that have shown comparison between hydrochloric acid and sulfuric acid in its use for acid hydrolysis. Hydrolysis with hydrochloric acid (HCl) is superior as it resulted in higher efficiency as compared to the one with sulfuric acid. Yustinah *et al.* (2012) reported that the use of HCl as catalyst, salts formed after neutralization of the yield are harmless salts, namely NaCl.

Most of the results above showed there was decrease in the resistant starch content on starch sources when it is treated dually with acid hydrolysis and annealing. Decrease in resistant starch content means its digestibility is increased. During acid hydrolysis, the oxygen in the glycosidic bond is attacked by the hydronium ion and thus the linkage is broken in the amorphous region initially due to the fragility of hydrogen bond in this area (Denardin and Silva, 2009; Silveira *et al.*, 2019). As a result, this increased the porosity of the granules (Pratiwi *et al.*, 2018). In this post-hydrolysis state, with addition step for annealing, where heat is introduced to these granules along with the excess water, will result in further destruction of the hydrogen bond between the polymers. Therefore, the resistant starch content will also further decrease. Sagum and Arcot (2000) reported that during the heating process, the hydrogen bonds linking amylose and amylopectin molecules weaken with increasing heating temperature. When the heat temperature increases, the water molecules have a higher kinetic energy so that they easily penetrate into the starch granules. Water will be bound simultaneously in the amylose and amylopectin molecules, resulting in decreased levels of resistant starch and increased digestibility. This effect can be greatly altered by several factors such as the type of acid used for acid hydrolysis (Angellier *et al.*, 2004), temperature, time of incubation, and the moisture content used for annealing. Although most studies have reported a decrease, an increase was also found in which it is of contradictory. O'Brien and Wang (2008) have suggested that the change in the porous structure of granules does not only decrease the enzymatic hydrolysis of starch but could also increase, and this depend on factors such as type of starch and type of enzyme being applied during the process.

3.5 Publication bias of meta-analysis

To draw conclusions about the overall risk of bias within or across trials it is necessary to summarise assessments across items in the tool for each outcome within each trial. The way that summary judgments of risk of bias are reached should be explicit and should be informed by empirical evidence of bias when it exists, likely direction of bias, and likely magnitude of bias (Higgins *et al.*, 2011). Based on Table 3, the value of Nft on the main parameter of this research is higher than calculation result of 5N +10. Therefore, this meta-analysis study is robust from possible publication bias.

Table 3. Publication bias analysis of meta-analysis using method of Rosenthal.

Parameter	N	Nft	5N +10
Dual modification of acid hydrolysis and annealing	9	534	55

N: Number of studies, Nft: Fail safe number

3.6 Meta-optimization using response surface methodology

The result of meta-analysis in this research continued to be further analysed in optimization methods using response surface methodology (RSM) to develop a precise approximate relationship between process variables (time of acid hydrolysis, annealing incubation temperature) and the outcome (resistant starch content). These parameters were used due to varied data to be processed using Design Expert Version 12 (Figure 7).

Figure 7 shows that all treatments (time of acid hydrolysis at 6, 30 and 78 h) and (annealing incubation temperature at 50, 60 and 70°C) decreased the resistant starch significantly. However, 6 h of acid hydrolysis and annealing incubation temperature at 50°C affect the smallest decrease in RS based on the top point of 3D surface graph when compared to 30 and 78 hrs of acid

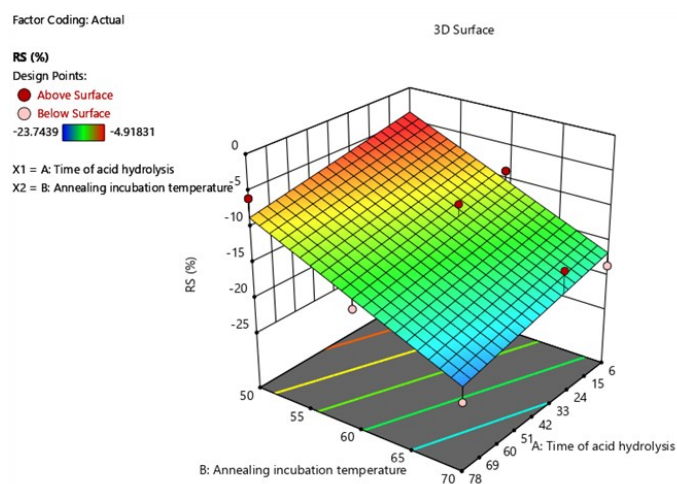


Figure 7. 3D surface graphic on the relationship between time of acid hydrolysis, annealing incubation temperature and resistant starch content.

hydrolysis and annealing incubation temperature at 60 and 70°C. This result is in line with the meta-analysis result as mentioned in Figure 5 (6 h of acid hydrolysis) and Figure 6 (50°C of annealing incubation temperature).

The RSM looks into an adequate approximation relationship between input and output variables and determined the best operating conditions for a system under study or a portion of the factor field that complies with the operating requirements (Farooq *et al.*, 2013). In numerous response surface scenarios, the researcher's focus lies in forecasting the response variable *y* or approximating the average response at a specific location within the space of process variables (Myers *et al.*, 2016). Optimization was done by RSM in a way that it only needs few experiments, in this case, only few studies chosen for meta-analysis, to study the effect of all the factors and the optimum/ideal combination of acid hydrolysis and annealing could be found. Consequently, their interactions could be determined in short time without having to conduct another trial experiment that takes a lot of time and cost.

4. Conclusion

The results revealed that HCl was deemed the most popular chemical in the treatment, mostly applied in corn starch. Dual modification of acid hydrolysis and annealing resulted mostly in the decrease of resistant starch content (62.5%) due to the changes in the porous structure of the amorphous region of the granules. MA and RSM are in line, showing that acid hydrolysis and annealing incubation for 6 h at 50°C showed the smallest decrease in RS.

Conflict of interest

The authors declare no conflict of interest.

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