Supplementary

Appendix 1 Search strategy summary in PubMed

SEARCH STRATEGY SUMMARY

- Date of search: [January 15, 2024-January 31, 2025]
- Databases searched: PubMed
- Search terms used in PubMed in various combinations:

("Blood Specimen Collection/instrumentation"[Mesh] OR "Blood Specimen Collection/methods"[Mesh] OR "Blood Specimen Collection/standards"[Mesh] OR "blood collection device*"[Title/Abstract] OR "blood specimen collection"[Title/Abstract])
("Anticoagulants"[Mesh] OR "Catheters"[Mesh] OR "Glycolysis"[Mesh] OR "Needles"[Mesh] OR "Gels"[Mesh] OR "Surface-Active Agents"[Mesh] OR "Syringes"[Mesh] OR anticoagulant*[Title/Abstract] OR catheter[Title/Abstract] OR "clot activator*"[Title/Abstract] OR "glycolysis inhibitor*"[Title/Abstract] OR needle*[Title/Abstract] OR "rubber stopper*"[Title/Abstract] OR gel*[Title/Abstract] OR surfactant*[Title/Abstract] OR syringe*[Title/Abstract] OR "tube wall*"[Title/Abstract])
("Biological Assay"[Mesh] OR "Blood Chemical Analysis/instrumentation"[Mesh] OR "Blood Chemical Analysis/methods"[Mesh] OR "Blood Chemical Analysis/standards"[Mesh] OR "Blood Preservation/adverse effects"[Mesh] OR "Blood Preservation/instrumentation"[Mesh] OR "Blood Preservation/methods"[Mesh] OR "Diagnostic Errors"[Mesh] OR "Equipment Contamination"[Mesh] OR "Immunoassay/methods"[Mesh] OR "Quality Improvement"[Mesh] OR "Specimen Handling"[Mesh] OR "blood analysis"[Title/Abstract:~2] OR "blood preservation"[Title/Abstract:~2] OR "test variability"[Title/Abstract] OR "test accuracy"[Title/Abstract] OR "test results" [Title/Abstract] OR error*[Title/Abstract] OR inaccuracy*[Title/Abstract] OR contamination*[Title/Abstract] OR "routine chemistry"[Title/Abstract] OR "specimen handling"[Title/Abstract:~2] OR immunoassay*[Title/Abstract])
("Humans"[Mesh])

- Timeframe: [January 1, 2014- January 31, 2025]

https://dx.doi.org/10.21037/jlpm-25-5

Table S1 Summary of original studies discussed in narrative review

Tube wall

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2020	Weikart	US	Experimental	Multiple experiments with varied replicates	Hybrid BCTs made of cyclic olefin polymer (COP) with internal silica coating had longer shelf-life, consistent draw volumes (<10% variation over 2 years), superior barrier properties, and high mechanical strength (no breakage after extreme stress)	COP-silica hybrid BCTs outperform PET tubes in shelf-life, draw volume consistency, mechanical integrity, and barrier properties	(12)
2021	Ladang	Belgium	Experimental	7	Tube wall composition altered amyloid-beta and tau adsorption, affecting Alzheimer's biomarker results	Tube wall materials should be standardized to ensure consistent Alzheimer's biomarker testing	(10)
2021	Strand	Norway	Experimental	14	Polypropylene tubes yielded greater beta-amyloid recovery than other materials; adsorption properties influenced biomarker levels	Standardized tube selection is key for reliable Alzheimer's biomarker analysis	(9)
2022	Yang	US	Experimental	45	BD Vacutainer EDTA tubes led to higher antimony contamination than Greiner sodium heparin tubes (mean +2.41 µg/L); low fill volumes exacerbated contamination (up to 33.7 µg/L), risking clinical misinterpretation	BD EDTA tubes pose a contamination risk for antimony testing; alternative validated tubes are recommended to avoid errors	(11)

https://dx.doi.org/10.21037/jlpm-25-5

Surfactants

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2015	Dorokhin	Netherlands	Experimental	Not specified	Nonionic surfactants (SFs), for example, Pluronic F-127, disrupted antibody–antigen binding in magnetic immunoassays. Higher concentrations of Pluronic F-127 SFs increased the effective dissociation rate of the immunoassay complex	SFs must be carefully selected to reduce immunoassay interference	(13)
2015	Kim	US	Experimental	Quality control (QC) samples (n=9), volunteers (n=5)	The authors developed ChemoPET, a base-catalyzed surface modification converting hydrophobic PET to hydrophilic without SFs, maintaining specimen integrity	ChemoPET BCTs offer a SF-free alternative to improve assay reliability	(14)
2016	Yu	China	Experimental	20	The study found that serum collected in Vacuette tubes with serum clot activator and gel yielded significantly higher 25-hydroxyvitamin D (25OH) D levels when analyzed using the Siemens Advia Centaur XP system compared to those measured by LC-MS/MS. The average bias was reported to be high, with a mean difference of 11.9 ng/mL. The authors hypothesized that the SFs in BCTs may have caused the overestimation in Advia vitamin D immunoassays	SF presence in tubes can bias results and requires consideration during assay validation	(17)
2016	Bowen	US	Experimental	60 volunteers and QC material	ChemoPET tubes without SFs demonstrated no significant interference in the measurement of cortisol, total triiodothyronine, total thyroxine, or routine assays. In contrast, SST and RST tubes may leach SFs into the blood specimen, which can affect assay results, unlike glass tubes, which do not contain SFs	Modified PET tubes without SFs are reliable for clinical chemistry testing	(15)
2018	Jalali Dil	US and Canada	Experimental	Not specified	Surface characterization of PET tubes revealed SF presence, leading to significant adsorption of free thyroxine (FT_4)	SFs in PET tubes can alter tests for thyroid function. BCT component evaluation is important to consider for laboratory testing	(16)
2024	Chae	South Korea	Experimental	4	Greiner Vacuette BCTs introduced bias (mean 9.95 ng/mL) in vitamin D immunoassays, leading to incorrect deficiency classifications. LC-MS/MS analysis showed no BCT-induced bias (<5%)	BCT-induced assay bias necessitates validation of BCTs for accurate vitamin D concentrations and to prevent misclassification of vitamin D deficiency	(18)

https://dx.doi.org/10.21037/jlpm-25-5

Stoppers and lubricants

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
1968	Baum	US	Experimental	30 (20 distilled water blanks, 10 blood specimens)	Glycerol lubricant used in Vacutainer tube stoppers significantly contaminated samples, increasing plasma glycerol levels. Distilled water blanks showed glycerol contamination in Vacutainer tubes but not in control tubes (<0.020 μmoles/mL in controls *vs.* up to 0.580 μmoles/mL in Vacutainers). Blood aliquots confirmed this glycerol contamination (up to 0.355 μmoles/mL in Vacutainers *vs.* 0.040 μmoles/mL in controls)	Glycerol in Vacutainer stoppers interfere with glycerol and triglyceride assays; tubes should be labeled or glycerol eliminated	(30)
1971	Chowdhury	US	Experimental	15 tubes	Commercial Vacutainer tubes contained significant glycerol-like contaminants (mean concentration 1.21 mM/tube), causing false elevation of plasma glycerol and triglyceride measurements	BCTs should be screened for glycerol contamination when measuring plasma lipids	(31)
1977	Borga	Sweden	Experimental	8	Plasma protein binding of basic drugs (alprenolol, imipramine) was significantly inhibited by tris (2-butoxyethyl) phosphate; (TBEP), a plasticizer from Vacutainer tube stoppers TBEP reduced alprenolol binding to α_1-acid glycoprotein from 76% to 16% at 10 μg/mL concentration and imipramine binding from 69% to 13% Significant variability of TBEP release from plastic tubes was observed, affecting clinical assays (correlation coefficient 0.86 for alprenolol, P<0.001; 0.66 for imipramine, P<0.01)	TBEP from Vacutainer stoppers disrupts drug-protein binding and biases plasma drug assays; such tubes should be avoided in TDM	(20)
1982	Shah	US	Experimental	Not specified	TBEP in some Vacutainer rubber stoppers causes significant interference in plasma drug measurements Affected drugs include basic, lipophilic compounds such as propranolol, lidocaine, quinidine, and tricyclic antidepressants The mechanism involves displacement of drugs from plasma protein binding sites and redistribution into red blood cells, leading to underestimation of drug concentration This interaction was reproducibly demonstrated using different tube contact conditions	The presence of TBEP in Vacutainer stoppers introduces clinically significant bias in TDM for specific drug classes Laboratories must confirm the absence of this plasticizer in tubes used for drug assays	(22)
1984	Devine	US	Experimental	Not specified	The plasticizer TBEP from synthetic rubber stoppers disrupted drug–protein binding significantly, reducing serum drug concentrations of quinidine by 11–32% and lidocaine by 10–18%, and increased free lidocaine levels significantly	TBEP contamination lowers total drug levels and increases free concentrations, potentially altering clinical decisions	(23)
2001	van den Besselaar	Netherlands	Experimental	Not explicitly stated (multiple experiments with various patient and normal plasma pools)	Magnesium was detected in Vacutainer tubes at 1.3–1.6 mmol/L Magnesium ions shortened prothrombin time (PT), particularly in coumarin-treated plasma Magnesium-induced PT shortening decreased the PT ratio and consequently the INR (INR reduction ranged from 0.9% to 6.6% in patients' samples with added magnesium)	Magnesium from stoppers shortens PT and lowers INR; manufacturers should prevent such contamination	(24)
2005	van den Besselaar	Netherlands	Experimental	78	Magnesium contamination from rubber stoppers was identified in Vacutainer tubes (1.1–1.5 mmol/L), not in Venoject II tubes. This contamination significantly shortened PT tests, with a more pronounced effect in anticoagulated patients. Depending on the coagulometer, magnesium contamination increased the International Sensitivity Index (3–6%), thereby artificially lowering the INR	Magnesium interference varies with coagulometer type but may cause clinically relevant INR shifts	(25)
2014	van den Besselaar	Netherlands	Experimental	87	Conventional rubber stoppers in sodium citrate tubes contained high magnesium levels, leading to shortened PT and INR values	Magnesium-free stoppers are preferred for reliable INR and coagulation testing	(26)
2019	Mason	US	Case Study	Not applicable	Magellan Diagnostics' LeadCare testing systems produce falsely low blood levels for venous samples	Improve labeling and instruction for use to minimize misinterpretation of blood lead results. Ensure the BCTs are periodically monitored with devices Any changes in manufacturing of BCT components should be communicated to *in vitro* diagnostics companies in a timely manner	(28)
2021	Kosecki	US	Experimental	10 from BCTs, 10 ampoules, and 7 from BCTs with deionized water =27 samples	Isobutylene contamination from conventional rubber stoppers in gray-top BCTs can mimic methanol in forensic alcohol analysis	Robust quality systems are essential to detect test inaccuracies; stopper formulation can affect test reliability	(27)
2021	Nakata	Japan	Experimental	994	The study compared blood lead levels using LeadCare and inductively coupled plasma mass spectrometry in 994 venous blood samples, revealing a significant positive bias in LeadCare at levels above 45 μg/dL The FDA warned that thiuram in certain BCTs can release gases that interfere with Pb measurements, potentially causing falsely low blood lead level results. The authors noted that these tubes were commonly used in their study before the FDA announcement	Awareness of stopper-related contamination is critical in forensic toxicology to avoid substance misidentification. Alternative BCTs should be used in lead testing to avoid interference from stopper-derived contaminants	(29)

https://dx.doi.org/10.21037/jlpm-25-5

Tube separators

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2017	Arslan	Turkey	Experimental	44	Significant bias was observed in AST, glucose, potassium, LDH, sodium, and total protein levels in Barricor tubes	Barricor tubes alter AST, potassium, LDH, glucose, and total protein compared to serum; LDH changes may reflect cellular lysis	(45)
2018	Padoan	Italy	Experimental	40	Barricor tubes had significantly lower residual white blood cells and red blood cells than PST tubes	Centrifuging Barricor tubes at 4,000g for 3 minutes improves plasma quality	(41)
2018	Fournier	Canada	Experimental	12	Barricor tubes showed comparable results to PST tubes for 50 analytes (bias –1.5% to 6.1%) and greater stability for AST, glucose, potassium, LDH (stable ≤10 days *vs.* <5 days in PST); lower platelet contamination (mean 2×10^9/L lower, P<0.05)	Barricor is a viable alternative to PST, with improved analyte stability and reduced cellular contamination	(42)
2019	Schrapp	France	Experimental	167 drugs	Use of BD PST™ II gel tubes caused significant reduction in concentrations of 40 drugs (antidepressants 11/26, neuroleptics 9/13, cardiovascular drugs 5/29, anxiolytics/hypnotics 4/25, drugs of abuse 5/26) Barricor™ tubes affected 6 drugs. Drugs with logP > 3.3 were especially unstable	Barricor tubes show less drug interference and are suitable for therapeutic drug monitoring (TDM)	(44)
2019	Wollmann	Norway	Experimental	3 patients (spiked serum samples) and 24 patients (real-life samples)	The study found that serum concentrations of 28 psychoactive drugs and 13 metabolites were significantly lower in samples stored on gel tubes compared to plain tubes after storage for 2 days. Specifically, the concentrations of lipophilic drugs were more affected by storage in gel tubes, with a strong correlation between residual concentrations and log P values. The measured concentrations of antiepileptic drugs were not significantly different between the two types of tubes	Gel separator tubes should be avoided for TDM of psychoactive drugs due to drug loss over time	(33)
2020	Hegstad	Norway	Experimental	21 antihypertensive drugs	The mean serum concentrations of 21 antihypertensive drugs showed no substantial concentration differences between gel and non-gel tubes at baseline. After 72 hours, concentrations of verapamil, lercanidipine, and canrenone in gel tubes containing 350 µL of serum were 35%, 88%, and 50% lower, respectively, compared to those containing 2 mL of serum. Statistically significant concentration changes exceeding 10% in gel tubes compared to non-gel tubes were noted	Most antihypertensives are stable in gel tubes, but drugs such as verapamil, lercanidipine, and canrenone require non-gel tubes	(46)
2020	Gawria	Sweden	Experimental	122	Phosphate and potassium were more stable in Barricor tubes (allowable bias exceeded at 68 hours and 40 hours, respectively, *vs.* 29–35 hours and 9–12 hours in gel tubes)	Barricor tubes enhance stability of labile analytes and mitigate hemolysis, which is especially valuable for remote or delayed processing	(43)
2020	Morosyuk	US & Europe	Experimental	705	BD Barricor tubes-maintained stability for 7 days for most therapeutic drugs, unlike PST tubes	Barricor tubes enhance drug stability for TDM	(47)
2021	Allard	US	Case Study	1	Improper gel barrier formation in SST despite proper centrifugation caused preanalytical errors, potentially affecting analyte stability and measurement accuracy	Improper gel barrier formation can compromise sample quality; visual inspection is recommended	(50)
2022	Knutti	Germany	Experimental	10	Amino acid and cytokine concentrations increased with prolonged storage in heparin and gel tubes	Barricor tubes reduce preanalytical delays while maintaining sample integrity	(48)
2022	Jordan	Canada	Experimental	40 paired samples per drug	Barricor (non-gel mechanical separator) tubes showed similar therapeutic drug levels to serum tubes. PST (gel-based separator) tubes showed negative bias for carbamazepine (–7.6%) and phenytoin (–6.8%), with stability issues observed, but did not exceed total allowable error of 10%. The stability study showed that all drugs recovered within 10% of baseline value when stored refrigerated for 7 days, except for some variations in phenytoin. Phenobarbital was stable in both Barricor and serum tubes but showed significant negative bias in PST tubes	Barricor is a reliable alternative to serum for TDM, while PST tubes may bias drug levels	(39)
2022	Shepard	Canada	Experimental	53	Up to 69% drug loss in gel tubes after 3 months, affecting forensic analysis	Drug adsorption in gel tubes must be considered in forensic toxicology assessments	(40)
2022	Bao	China	Observational	Not specified	Serum calcium levels were significantly higher in samples collected using a new batch of vacuum BCTs (s2005030) compared to an old batch (s2001006). The calcium concentration in the new batch was inversely proportional to the amount of deionized water added, indicating contamination from the separator gel	Elevated calcium levels in new BCT batches were caused by gel contamination; batch verification is essential	(51)
2023	Cembrowski	Canada	Retrospective cohort study analysis	PST from May 2015 to April 2018, (n=59,762 specimens) and Barricor May 2018 to May 2021, (n=61,512 specimens)	Barricor tubes reduced intra-patient variation in troponin and chloride compared to PST tubes. The percentage of hs-TnT outliers was significantly lower in Barricor (8.32%) than PST (12.2%, P<0.001).	Laboratories should verify each new batch of separator tubes to ensure accuracy and prevent adverse outcomes. Barricor tubes reduce variability in hs-TnT and chloride *vs.* PST by producing cleaner plasma	(49)
2023	Garza	US	Experimental	21	18 out of 21 drugs were stable in gel-containing tubes, 3 drugs (total tricyclics, lidocaine, free phenytoin) were affected by gel separator in BCTs	Gel-containing BCTs are useful for testing many therapeutic drugs under typical storage conditions and help improve laboratory workflow	(34)
2023	Tokudome	Japan	Experimental	3	Serum separation gels adsorb certain drugs, leading to decreased plasma drug concentrations. Significant decreases in concentrations of amitriptyline, chlorpromazine, and flunitrazepam were observed, even in control tubes Positive correlation was observed between logP values and percentage decreases in drug concentrations for Vacutainer (r=0.96, P=0.01) and Insepack (r=0.94, P=0.02); no correlation for Neotube (r=0.88, P=0.052) or Venoject (r=0.80, P=0.10)	Tubes without separators are preferred for TDM and toxicology to minimize drug loss	(38)

https://dx.doi.org/10.21037/jlpm-25-5

Clot activators

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2014	La'ulu	US	Experimental	10	Significant thrombin-mediated degradation of parathyroid hormone (PTH) occurred in rapid serum tubes (RSTs, containing bovine thrombin) compared to PST and SST, with rate constants faster in RSTs, followed by SSTs, and least in PSTs	Thrombin present in BCTs can cause clinically relevant false decreases in measured intact PTH concentrations, with more severe effects in tubes containing exogenous bovine thrombin	(54)
2015	Naznin	Bangladesh	Experimental	40	Silica clot activator and silicone SF in plastic vacutainer tubes caused significant interference with lithium estimation by ion-selective electrode (ISE), falsely elevating lithium concentrations significantly compared to plain tubes without additives	Silica clot activators and silicone SFs significantly interfere with lithium estimation by ISE, causing clinically significant preanalytical errors; plain tubes without additives are recommended for accurate lithium measurement	(56)
2018	Ikkurthi	India	Experimental	100	Serum lithium levels from clot-activator vacutainers showed significantly higher positive bias (mean bias 19.9%) compared to glass vials. Sodium heparin plasma was comparable with glass vials (3.34% bias). Stability of lithium in storage was highest in glass vials	Glass vials should be preferred for lithium estimation; clot-activator tubes may falsely elevate lithium levels	(57)
2022	Zhao	Australia	Experimental	Not explicitly stated	Recombinant ecarin (rEcarin) was successfully cloned and expressed in mammalian cells. It demonstrated comparable clotting efficiency to native ecarin (N-Ecarin) and was effective in clotting both normal and anticoagulated blood, providing high-quality serum	Recombinant ecarin has strong potential as an additive in BCTs for producing high-quality serum, offering advantages over snake venom-derived activators.	(59)
2023	Sahu	India	Experimental	100	Clot activator tubes significantly lowered lithium measurements compared to plain glass tubes when analyzed by reflectance photometry (VITROS 4600). Stability over 48 hours was unaffected by tube type	Lithium estimation in clot activator tubes is significantly lower than in plain glass tubes. Glass tubes are recommended to ensure accurate lithium monitoring	(55)
2023	Saharia	India	Experimental	51	Lithium measurement significantly differed across tubes, with clot activator tubes (BD Vacutainer and Xinle tubes) causing elevated lithium results compared to glass tubes. Significant preanalytical interference and imprecision occurred particularly with Xinle tubes	Lithium estimation accuracy is compromised in clot-activator tubes due to positive interference; glass tubes are recommended for accurate lithium estimation	(58)
2024	Zhao	Australia	Experimental	5	The recombinant activated protein clot (RAPClot) prototype tube using recombinant ecarin (from snake venom) demonstrated efficient clotting even in anticoagulated blood. It retained high enzymatic activity after sterilization and storage, and preliminary clinical trials showed comparable results to commercial BCTs	The RAPClot blood collection prototype tube has significant potential for routine clinical use, with advantages over current serum or lithium heparin plasma tubes in biochemical analyte measurement	(60)

https://dx.doi.org/10.21037/jlpm-25-5

Heparin

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2014	Chhapola	India	Experimental	35	Liquid heparin (LH) significantly affected blood gas results unlike dry balanced heparin (DBH), causing discrepancies beyond allowable error limits (LOA) for pCO_2, pO_2, HCO_3^-, Na^+, K^+, and Cl^-. Only pH and lactate were comparable between LH and DBH.	Liquid heparin should not be considered interchangeable with DBH syringes for blood gas analysis except for pH and lactate, due to significant preanalytical errors	(64)
2022	Jiang	China	Experimental	34	Heparin in BCTs led to significantly higher tau and p-tau181 levels compared to EDTA tubes; no significant effect was observed on the Aβ1–42 to Aβ1–40 ratio	BCT type should be considered in studies measuring plasma tau levels to avoid misinterpretation	(63)
2023	Jacobs	Belgium	Experimental	34	Heparin plasma tubes showed significant interference in 25-OH-Vitamin D measurement on Liaison XL analyzer, causing overestimation of values	Heparin plasma tubes are unsuitable for accurate 25-OH-Vitamin D assessment using the Liaison XL analyzer due to significant bias	(62)
2023	Mahler	US	Experimental	8	Underfilled heparin tubes caused significant pH to increase and ionized calcium decrease; lactate and potassium levels were unaffected	Venous blood-gas specimens in heparin tubes should be filled to at least 2/3 full to ensure accurate pH and ionized calcium readings	(61)

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EDTA

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2014	Lima-Oliveira	Italy & Brazil	Experimental	15	Even minor EDTA contamination (5%) caused significant biases in calcium, magnesium, potassium, and lactate dehydrogenase levels	EDTA contamination must be minimized to prevent erroneous biochemical test results	(66)
2015	Cadamuro	Austria	Experimental	10	EDTA carryover was unlikely in closed vacuum systems but was observed with syringe blood transfer, altering magnesium and calcium levels	Strict adherence to recommended phlebotomy techniques is necessary to prevent EDTA-related sample contamination	(92)
2016	Toprak	Turkey	Experimental	Not explicitly stated	Higher EDTA concentrations significantly reduced ACTH assay results	Inadequately filled EDTA tubes should be rejected for ACTH testing	(67)
2022	Jiang	China	Experimental	34	K2-EDTA tubes yielded significantly lower plasma tau and p-tau181 levels than Li-Hep and Na-Hep tubes, while the 3 ratios Aβ1–40, Aβ1–42, and Aβ1–40 to Aβ1–42 ratio were unaffected	The choice of BCT affects tau biomarker quantification; standardization is necessary for Alzheimer's disease biomarker research	(63)

https://dx.doi.org/10.21037/jlpm-25-5

Citrate

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2019	Calcoen	Belgium	Case Report	Not specified	Coagulation error messages linked to clotted citrate tubes increased abruptly; preanalytical errors related to improper filling and lot-dependent additive variations were identified	Preanalytical vigilance is critical; laboratories should monitor clotting rates in citrate tubes and ensure quality control to avoid erroneous coagulation test results	(69)
2021	Gosselin	US	Guidance or Expert Opinion	Not applicable	Sodium citrate coagulation tubes were in short supply due to manufacturing issues and increased demand; variability among manufacturers affects test reliability	Laboratories should validate new citrate tube sources, avoid substandard alternatives, and ensure proper blood-to-citrate ratios for accurate hemostasis testing	(71)
2023	Gros	Slovenia	Experimental	Not specified	Citrate concentration in BCTs varied, affecting coagulation test accuracy	The spectrometric methodology offers a low-cost, easy-to-apply approach for evaluating anticoagulant concentrations in BCTs. This enables better insight into preanalytical variables, such as anticoagulant concentrations affecting coagulation results, and may assist in standardizing BCTs and laboratory results	(70)

https://dx.doi.org/10.21037/jlpm-25-5

Glycolysis inhibitors

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
1989	Chan	Hong Kong	Experimental	45	Sodium fluoride (NaF) effectively preserved glucose concentrations for up to 72 hours. Glucose concentrations decreased rapidly initially in both NaF and heparin tubes, stabilizing after 4 hours in NaF tubes	NaF is effective but initially slow to act. Immediate separation of plasma from cells is crucial when immediate glucose measurement is not feasible	(75)
2014	Szoke	Italy	Experimental	50	Citrate-buffered tubes provided higher glucose concentrations than NaF tubes, leading to reclassification of 23% of patients	Switching to citrate tubes requires re-evaluation of glucose cutoffs to avoid overdiagnosis of diabetes	(81)
2015	Dimeski	Australia	Experimental	42	Glucomedics tubes (NaF/KOx, citrate, EDTA) were the most effective in preventing glycolysis for up to 4 hours at room temperature. A correction for dilution factors was required	Glucomedics tubes provide the highest accuracy for glucose estimation by minimizing glycolysis	(82)
2016	Bonetti	Italy	Experimental	49	Sodium fluoride/citrate buffer tubes prevented glycolysis more than NaF or lithium-heparin tubes	GlucoEXACT tubes (NaF-citrate buffer) effectively prevent glycolysis, making them suitable for routine glucose testing	(76)
2018	Saracevic	Croatia	Experimental	40	Glucose concentrations varied significantly between different glycolysis inhibitor-containing tubes, with biases up to 7.3%	Different glycolysis inhibitor tubes cannot be used interchangeably due to clinically significant biases	(83)
2018	Balboni	Italy	Experimental	60	Glucose in lithium-heparin tubes decreased faster than in serum tubes at RT; refrigerated samples showed better stability	Serum tubes allow delayed glucose measurement up to 96 hours, but lithium-heparin tubes require prompt analysis	(79)
2018	Banerjee	India	Experimental	15	D-Mannose (3 mg/mL) preserved glucose better than NaF and did not interfere with most analytes except potassium	D-Mannose is a promising antiglycolytic agent for blood glucose preservation	(84)
2019	Coward	UK	Experimental	Not specified	Barricor and FC-Mix tubes preserved glucose better than traditional NaF/EDTA tubes	Newer technologies such as Barricor and FC-Mix tubes improve glucose stabilization and laboratory efficiency	(85)
2020	Jung	US	Experimental	Not specified	Sodium fluoride was more effective than sodium citrate and heparin in inhibiting glycolysis with delayed processing	Sodium fluoride remains the best option for stabilizing glucose in delayed sample processing	(78)
2020	Potter	Australia	Observational	7,509	The change from delayed to early centrifugation of OGTT blood samples significantly increased GDM diagnosis rates. Early centrifugation raised OGTT fasting glucose by 0.24 mmol/L (5.4%), 1 hour by 0.34 mmol/L (4.9%), and 2 hours by 0.16 mmol/L (2.3%) (P<0.0001), nearly doubling the GDM diagnosis rate from 11.6% to 20.6%	Preanalytical processing of OGTT blood samples is critical for accurate GDM diagnosis; standardization is needed	(72)
2020	Loganathan	India	Experimental	40	NaF-Na2EDTA tubes had better glycolysis inhibition than serum and NaF tubes	NaF-Na2EDTA tubes should be more widely adopted to prevent preanalytical errors in glucose testing	(77)
2021	Szoke	Italy	Experimental	578	Citrate-buffered tubes increased GDM prevalence from 11.9% to 27.5%	Citrate-buffered tubes enhance GDM detection, but potential overdiagnosis must be balanced with clinical outcomes	(86)
2024	Kume	Japan	Experimental	10	NaF-ATP tubes showed reduced glucose decline over 24 hours compared to standard NaF tubes	NaF-ATP tubes improve glucose stability and could be beneficial for long-term sample storage	(88)
2024	Nevraumont	Belgium	Experimental	701	Citrate-containing tubes stabilized glucose more than NaF tubes, leading to an 84% increase in IFG and 150% increase in GDM diagnoses	Citrate-containing tubes offer long-term glucose stability but may require revised diagnostic thresholds	(87)
2024	Backman	Sweden	Substudy of a GDM multicenter, randomized, controlled trial	65	Citrate tubes showed increased glucose concentrations (+0.08 mmol/L) compared to NaF tubes; GDM prevalence was 9.1% higher with citrate tubes	Citrate tubes provide higher glucose measurements and higher prevalence of GDM than NaF tubes	(146)
2024	Bakkebo	Norway	Experimental	30	NaF-EDTA-citrate plasma overestimated glucose by 4.7% compared to lithium-heparin plasma; fast-clotting serum tubes were equivalent to lithium-heparin plasma	Fast-clotting serum tubes could be an alternative for glucose measurement in GDM and diabetes diagnosis	(74)
2024	Heilmann	Germany	Clinical	578	NaF-citrate plasma showed 4.72% higher glucose values than whole blood; estimated diabetes prevalence increased by 13.67%	NaF-citrate tubes require new conversion factors to avoid overestimation of diabetes prevalence	(89)

https://dx.doi.org/10.21037/jlpm-25-5

Order of draw

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2015	Simundic	Europe (multi-country)	Observational	336 audits across 12 countries	Errors in phlebotomy procedures, including stopper-related issues, contributed to preanalytical variability in clinical testing	Strict adherence to standardized blood collection protocols is necessary to mitigate preanalytical errors caused by stoppers and other factors	(19)
2015	Cadamuro	Austria	Experimental and Observational	10	EDTA carryover was unlikely in closed vacuum systems; contamination required severe protocol neglect	Adherence to recommended practices ensures no significant impact on biochemical results.	(92)
2018	Jacobsen	Denmark	Observational	49 departments	Moderate adherence (63.3%) to CLSI and WHO guidelines were observed among Danish laboratories blood collection practices	Significant variability exists in blood tube collection practices among Danish laboratories, indicating moderate compliance with international guidelines and highlighting the need for standardized, evidence-based blood collection practices	(147)
2019	Keppel	Austria	Experimental	Simulated phlebotomy experiments: sample numbers varied by experiment	Citrate and heparin contamination during standardized blood draws were unlikely but possible with deviations from guidelines. Clinically significant contamination effects noted in ionized calcium, coagulation parameters (aPTT, PT) at minimal contamination volumes (5–100 µL)	Strict adherence to phlebotomy guidelines is critical; minor carryover contamination can have significant clinical impacts	(94)
2021	Ercan	Turkey	Cross-sectional	793	Incorrect order of draw did not cause K-EDTA contamination, but order of draw influenced potassium results	Potassium variation is independent of contamination, suggesting order of draw affects results in closed systems	(93)
2022	Mahato	India	Observational Cross-sectional	120 nurses surveyed	Nurses lacked adequate awareness of order of draw; errors in technique were common	Training is essential to minimize preanalytical errors affecting clinical results	(95)
2024	Mahto	India	Case Series	4 cases	Preanalytical errors led to incorrect coagulation results, often due to sample mishandling or contamination	Strict adherence to order of draw and sample handling guidelines is necessary to prevent spurious results	(96)

https://dx.doi.org/10.21037/jlpm-25-5

Metabolomics

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2013	Yin	China/ Germany	Experimental	Not specified	Blood tube additives significantly affected the EDTA plasma metabolome (notably hypoxanthine and sphingosine-1-phosphate) after 2 hours at room temperature; cooling reduced this instability. Hemolysis altered metabolite profiles significantly; freeze–thaw cycles caused minor changes	For accurate metabolomics, test tubes should be validated, hemolysis avoided, samples cooled immediately, EDTA plasma used, and freeze–thaw cycles limited	(111)
2016	Lopez-Bascon	Spain	Experimental	Not specified	Polymeric gel tubes altered metabolomic levels in serum (changes in alanine, proline, threonine, glycerolipids, aconitic acid, lactic acid) but not plasma	Polymeric gel tubes require careful evaluation in metabolomics applications to minimize bias	(114)
2019	Needham	US	Experimental	Not specified	Separator gel tubes (BD SST) caused significant interference in NMR lipoprotein subclass analysis, particularly affecting LDL-p, HDL-p, and VLDL measurements. Smaller fill volumes enhanced interference. Minimal interference was seen in conventional lipid assays	Consistent tube type and fill volume are critical for metabolomics accuracy	(102)
2020	Zhang	China	Experimental	12	Coagulant tubes significantly altered the serum proteomic profile compared to non-additive tubes, especially in healthy controls (27 significant peaks altered), minimally affecting patient samples (1 significant peak altered). Coagulants altered biomarker expression levels, affecting diagnostic interpretation.	BCT type directly affects biomarker detection; tube selection must be deliberate	(103)
2021	Sotelo-Orozco	US	Experimental	50	Serum and plasma types varied in metabolite content due to anticoagulants	Tube selection affects large-scale metabolomics studies and should be standardized. The use of the same type of additives in BCTs is important to minimize the variability in results from metabolomic profiles	(113)
2021	Kennedy	US	Experimental	27 donors; 135 total samples	Significant differences in metabolomic profiles were observed across different anticoagulants (EDTA, lithium heparin, sodium citrate) and serum. EDTA plasma had significantly fewer biochemical changes than serum and other anticoagulants; whole blood exhibited the greatest differences	Consistency in anticoagulants and additives is key due to biochemical variability	(105)
2022	Vignoli	Italy	Experimental	6	BCTs significantly alter metabolomic and lipoprotein profiles	Statistical adjustments can correct for tube-related effects in metabolomics data	(106)
2023	Yuan	China	Experimental	Not specified	EDTA vacutainers introduce small molecule contamination, affecting metabolite quantification and causing false biomarker discovery	Removing background metabolites improves reliability in biomarker identification	(112)
2023	Smit	Netherlands	Experimental	44	Quantitative protein mass spectrometry results were significantly affected by anticoagulants. Citrate plasma showed a bias of –14.6% due to dilution, EDTA plasma –5.3% due to reduced digestion efficiency, while heparin plasma was comparable to serum (–0.3% bias)	Standardized preanalytical protocols are vital for quantitative proteomics; heparin plasma is preferable, while citrate and EDTA should be limited. Using blank tubes before biomarker identification is vital	(107)
2024	Canez	Canada	Experimental	Not specified	Polypropylene tubes introduced contamination, affecting lipid quantification and identification (ion suppression)	Plastic leachates (polypropylene) compromise lipidomics; glass containers are recommended	(110)

https://dx.doi.org/10.21037/jlpm-25-5

Proteomics

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2016	Lopez-Bascon	Spain	Experimental	Not specified	Polymeric gel tubes affect metabolite levels in serum more than in plasm	Serum in polymeric gel tubes should be carefully considered for metabolomics studies	(114)
2017	Ilies	Romania and Germany	Experimental	6	Heparin plasma had a high number of detectable proteins and low variance; EDTA and citrate plasma differed significantly in protein profiles	The choice of blood collection method significantly affects proteomic profiles; heparin plasma may be optimal for proteomics	(100)
2021	Halvey	US	Experimental	324	Delayed centrifugation had a major impact on proteomic variability; storage temperature and anticoagulant choice also influenced results	Standardized blood processing is crucial to ensure reliable plasma proteomic analyses	(101)
2022	Vignoli	Italy	Experimental	6	BCTs significantly altered metabolic and lipoprotein profiles	Serum and plasma collection tubes must be standardized for reliable proteomics and metabolomics studies	(106)
2024	Li	US	Screening	24	Medical collection devices leach environmental chemicals such as phthalates and parabens, which may contaminate proteomic analyses	Prescreening of collection materials is necessary to prevent contamination in clinical proteomics	(148)

https://dx.doi.org/10.21037/jlpm-25-5

Validation and verification of blood collection tubes

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2017	Chung	South Korea	Experimental	100	Improve Medical Improvacutor tubes met CLIA 88 and Ricos performance goals for most analytes. Potassium bias after 72 hours storage was lowest with Improvacutor tubes compared to Greiner Vacuette and BD Vacutainer BCTs	Improvacutor tubes are reliable for routine chemistry; selection of tubes can affect analytic performance, especially under storage conditions	(125)
2020	Ucar	Turkey	Technical Validation	150	BD Barricor plasma tubes performed comparably to traditional SST; minor concerns were reported with white particulate matter	Local validation of new tubes should be conducted to ensure their suitability for clinical use	(119)
2021	Gosselin	US	Guidance/ Expert Opinion	Not applicable	A shortage of 3.2% sodium citrate coagulation tubes was reported due to manufacturing issues and increased demand; variability among manufacturers affects test reliability	Laboratories should validate new citrate tube sources, avoid substandard alternatives, and ensure proper blood-to-citrate ratios for accurate hemostasis testing	(71)
2023	Nell	South Africa	Multicenter Verification	300	Different BCTs introduced variability in hematology results; verification was necessary to ensure accuracy	A single tube brand should be used in laboratories to maintain consistency in hematology results	(121)
024	Abusoglu	Turkey	Experimental	50 (20 controls, 30 patients	Vacusel and BD serum tubes exhibited similar performance in 20 out of 23 clinical chemistry parameters; minor deviations were reported in LDH, Na, and total protein	Vacusel tubes offer acceptable performance and could be an alternative to BD tubes for clinical chemistry testing	(120)

https://dx.doi.org/10.21037/jlpm-25-5

Catheters

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2000	Moss	UK	Randomized controlled trial	204	Drawing blood through benzalkonium chloride-coated catheters may cause minor elevations in sodium and potassium	Electrolyte testing via these catheters should be interpreted cautiously. Catheter coatings may affect test accuracy	(129)
2014	Hacker	Germany	Experimental	15 patients and 26 central venous catheters (in vitro)	Central venous catheters previously used for cyclosporine or tacrolimus can falsely elevate drug levels due to reversible adsorption.	Direct venipuncture with a fresh needle is necessary for accurate TDM; reuse of catheters should be avoided	(132)
2017	Cadacio	US	Experimental	30	PIVO, a needle-free blood collection device, provided blood sample integrity comparable to venipuncture, with no hemolysis or clotting	The PIVO device is a promising alternative to venipuncture, potentially improving patient comfort and reducing risks associated with traditional blood draws	(134)
2018	Natali	US	Prospective and retrospective analysis	~7600 draws (2380 analyzed)	The PIVO device showed a 39% lower hemolysis rate than venipuncture and central line collection	Needle-less PIVO draws reduce hemolysis risk and may be a superior method for laboratory sample integrity	(135)
2021	Kader	Turkey	Experimental	44	No significant difference was observed in hemolysis index or laboratory parameters (K, AST, LDH) between Eclipse needle and Ultra-Touch butterfly sets	Eclipse and Ultratouch needles are safe for use in routine testing without increasing hemolysis risk	(126)
2022	Marschner	US	Case report	1 case	Blood collection from catheters used to infuse IV tacrolimus produce elevated tacrolimus concentrations even 27 days after last IV administration of the drug	Blood draws for tacrolimus should be from peripheral venipuncture to avoid false increases in blood tacrolimus from IV catheter previously used to infuse IV tacrolimus	(133)

https://dx.doi.org/10.21037/jlpm-25-5

Syringes

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2012	Lima-Oliveira	Italy/Brazil	Experimental	100	Different syringe types (heparin types) affected blood gas and electrolyte results significantly	Syringe material and preparation affect laboratory results, highlighting the importance of device selection during venous sampling	(138)
2022	Cuhadar	Turkey	Experimental	20	Blood gas analysis results remained stable for up to 60 minutes at room temperature but degraded with prolonged storage, especially with air contamination	Immediate analysis is recommended for arterial blood gases; air bubble contamination must be minimized to ensure accuracy	(136)
2023	Zavorsky	US	Experimental	200	Blood gas stability was affected by storage time and temperature; slushed ice reduced pO2 stability compared to room temperature storage	For optimal blood gas analysis, samples should be analyzed within 40 minutes at room temperature; ice storage is not recommended for pO2 stability	(137)

https://dx.doi.org/10.21037/jlpm-25-5

Needles

Year	First author	Country	Study design	Sample size (n)	Key findings	Conclusions	References
2020	Laur	Germany / Switzerland	Experimental	Not specified	The study did not explicitly demonstrate significant contamination from either stainless steel or plastic needles	Needle material (stainless steel *vs.* plastic) was acknowledged by the authors as a potential source of trace metal contamination; however, no direct evidence of contamination was found or reported in their study	(139)
2021	Sommer	US	Experimental	100	No significant contamination from stainless steel needles was found. Chromium and cobalt levels remained stable over 1 year	Contamination control is crucial in trace element analysis. Stainless-steel needles do not significantly leach metals	(140)
2024	Umemura	Japan	Retrospective	Not specified	Finer needles reduced persistent pain but increased hemolysis, affecting laboratory test results	Needle gauge selection should balance patient comfort with maintaining sample integrity	(144)
2024	Lippi	Italy	Experimental	15	Needle diameter variability affected blood flow and risk of hemolysis	Needle selection plays a critical role in preventing preanalytical errors in laboratory testing	(143)
2024	Rosada	Germany	Experimental	161	66.5% of patients had anemia, and 5% had hyperkalemia. Pain perception was similar between UltraTouch™ Push Button (UT-PB) and Safety-Lok™ (SL) devices. UT-PB showed 16–22% less hematoma development (not statistically significant) and a 47% lower hemolysis index than SL	Both BCDs perform similarly in terms of sample quality. The UT-PB device may offer slight advantages in handling comfort for phlebotomists, suggesting its potential utility in clinical settings, particularly for patients with difficult venous access	(145)
2024	Giussani	Italy	Observational prospective	577	Patients experienced significantly lower pain perception and anxiety levels when using the UltraTouch™ Push Button Blood Collection Set (UT-PBBCS) with smaller-gauge needles (23G and 25G) compared to the Standard Low-Volume Blood Collection Set (SLBCS) with larger-gauge needles (21G and 23G) ($P<0.001$). Despite using smaller-gauge needles, the hemolysis rates in samples collected with the UT-PBBCS were lower than those collected with the SLBCS, indicating that sample quality was maintained ($P<0.001$)	Down-gauging blood collection needles enhances patient comfort while maintaining sample integrity. The UT-PBBCS is effective for oncology patients	(142)

Aβ, amyloid beta; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BCT, blood collection tube; BD, Becton–Dickinson; CLIA, Clinical Laboratory Improvement Amendments; CLSI, Clinical Laboratory and Standards Institute; COP, cyclic olefin polymer; DBH, dry balanced heparin; EDTA, ethylenediaminetetraacetic acid; FT4, free thyroxine; GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; ISE, ion-selective electrode; K-EDTA, potassium ethylenediaminetetraacetic acid; LC-MS/MS, liquid chromatography–tandem mass spectrometry; LH, liquid heparin; LDL, low-density lipoprotein; LOA, limits of agreement; N-Ecarin, native ecarin; NMR, nuclear magnetic resonance; PTH, parathyroid hormone; PST, plasma separator tube; QC, quality control; RST, rapid serum tube; rEcarin, recombinant ecarin; SF, surfactant; SST, serum separator tube; TBEP, tris(2-butoxyethyl)phosphate; TDM, therapeutic drug monitoring; tau, tau protein; p-tau181, phosphorylated tau protein; Aβ1–42, amyloid beta 1-42; Aβ1–40, amyloid beta 1-40; WHO, World Health Organization.

https://dx.doi.org/10.21037/jlpm-25-5